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2,4,5-T: Position Document 2/3

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U.S. Environmental Protection Agency
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This Position Document addresses the risks and benefits of pesticide products containing the subject active ingredient. The Agency has determined that the use of products containing the subject active ingredient may meet or exceed a risk criterion described in 40 CFR Part 154. Potential hazards will be examined further to determine the nature and extent of the risk, and considering the benefits of the subject active ingredient, whether such risks cause unreasonable adverse effects on the environment.

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I. INTRODUCTION

On April 11, 1978, the Environmental Protection Agency (EPA) issued a notice of rebuttable presumption against all registrations of the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) [43 FR 17116, 21 April 1978]. Issuance of the RPAR began the Agency's public review of the risks and benefits of all uses of this chemical. On February 28, 1979, responding in part to information developed through the RPAR, the Administrator ordered the emergency suspension of the use of 2,4,5-T on forests, rights-of-way, and pastures ("suspended uses") [44 FR 15874, 15 March 1979]. At the same time, the Administrator also issued notices of intent to cancel these uses. These actions terminated the RPAR review of the suspended uses of 2,4,5-T and initiated public hearings on issues relating to the risks and benefits of these uses.*/

The Agency continued to review the use of 2,4,5-T on rangeland, rice, and non-crop areas**/ ("non-suspended uses") and has concluded that, when used in accordance with widespread and commonly recognized practice, the non-suspended uses of 2,4,5-T appear to cause unreasonable adverse effects on the environment. As a result, the Agency is issuing a notice of intent to hold a hearing to determine whether the non-suspended uses of 2,4,5-T should be cancelled.

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*/ Suspension proceedings began on April 19, 1979, but were discontinued on May 15, 1979 after all registrants withdrew from the hearings. The first pre-hearing conference for the cancellation proceedings was held on June 5, 1979; the formal hearing will probably begin in the fall.

**/ The non-crop uses of 2,4,5-T include use at the following sites: airports; fences, hedgerows (not otherwise included in suspended uses, e.g., rights-of-way, pasture); lumber yards; refineries; non-food crop areas; storgage areas; wastelands (not otherwise included in suspended uses, e.g., forestry); vacant lots; tank farms; industrial sites and areas (not otherwise included in suspended uses, e.g. rights-of-way).

This Position Document reviews the Agency's assessment of the risks and benefits of the non-suspended uses of 2,4,5-T, particularly use on rice and rangeland, and explains the bases for the Agency's decision to terminate the RPAR for these uses by convening a hearing to determine whether or not to cancel these uses.

This Position Document contains five parts. Part I, this introduction, summarizes the legal provisions relating to the RPAR review and cancellation of pesticides, and background information on the chemistry and uses of 2,4,5-T. Part II is the Agency's analysis of rebuttal comments submitted in response to the risks cited in Position Document 1. Part III is an evaluation of the data and information relating to the risks associated with the non-suspended uses of 2,4,5-T. This part includes the Agency's analysis of laboratory data, other new data and information developed through the RPAR review, information on exposure potential, and other risk considerations. Part IV reviews the benefits associated with the non-suspended uses of 2,4,5-T on a use-by-use basis and discusses the data on risks in light of the data on benefits. Part V contains the Agency's regulatory determination and explains the bases for the determination that a hearing on the risks and benefits of these uses is the most appropriate way to terminate the RPAR.

A. Legal Authority

(1) Statutory Provisions

The Federal Insecticide, Fungicide, and Rodenticide Act, as amended ("FIFRA") [7 U.S.C. 136 *et seq*.] requires the Environmental Protection Agency (EPA) to regulate all pesticide products through review of the risks and benefits of the uses of these chemicals. A key provision is Section 12(a)(1)(A) of FIFRA which specifies that all pesticide products must be registered by the Administrator before they may be sold or distributed. Before a pesticide may be registered, however, the Administrator must determine that its use will not result in "unreasonable adverse effects on the environment," defined in Section 2(bb) of FIFRA as "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide." In other words, any decision on pesticide registration must take into account both risks and benefits from the pesticide's use.

Under Section 6(b) of FIFRA, the Administrator may cancel the registration of a pesticide or change its terms and conditions of registration if it appears that the pesticide, "when used in accordance with widespread and commonly recognized practice, generally causes unreasonable adverse effects on the environment." For example, the Administrator may cancel the registration of a pesticide or change its terms and conditions of registration, if its labeling does not comply with the misbranding provisions of FIFRA which require the labeling to contain language "adequate to protect health and the environment" [FIFRA 2(q)].

Two types of proceedings are available under Section 6(b) of FIFRA to cancel a pesticide registration, or to modify the terms and conditions of its registration: FIFRA Section 6(b)(1) proceedings and FIFRA Section 6(b)(2) proceedings. In general, FIFRA Section 6(b)(1) proceedings begin with a notice specifying the regulatory action which the Administrator is proposing. This action takes effect automatically, without hearings, at the expiration of a notice period prescribed by statute, unless the registrants or a person adversely affected by the notice requests a hearing within that period. If a hearing is requested, the regulatory action proposed by the Administrator does not take effect; however, at the conclusion of the hearing, the Administrator may implement the proposed action, if he determines that it is appropriate to do so based on the record developed in the hearing.

Section 6(b)(2) proceedings, on the other hand, begin with a general notice specifying the issues which the Administrator desires to have explored at a hearing. Unlike Section 6(b)(1) proceedings, the Section 6(b)(2) proceeding does not include an initial proposed regulatory solution which would take effect automatically if a hearing is not requested. Interested persons may participate in the hearing; at the conclusion of the hearing, the Administrator may take whatever action he deems appropriate, based upon the record developed in the hearing, including cancellation of a pesticide registration or modification of the terms and conditions of its registration.

(2) The "RPAR" Process

The Rebuttable Presumption Against Registration (RPAR) process provides a mechanism through which the Agency gathers risk and benefit information about pesticides which appear to pose risks of adverse effects to human health or the environment which may be unreasonable. Through this process, the Agency invites pesticide registrants, environmentalists, and other interested persons to participate in the Agency's review of suspect pesticides in order to reach an open and balanced decision on the continued use of the pesticides.

The RPAR regulations at 40 CFR 162.11 (a)(3) prescribe regulatory criteria for the Agency's preliminary assessment of a pesticide's health and environmental effects and provide that an RPAR shall arise if the Agency determines that any of the risk criteria have been met. The Agency generally announces that an RPAR has arisen by publishing a notice in the Federal Register. Once a rebuttable presumption has arisen, registrants, applicants, and interested persons may submit evidence in rebuttal or in support of the presumption. Information on the economic, social, and environmental benefits of any use of the pesticide may also be submitted.

If the presumptions of risk are not rebutted, the benefits evidence submitted and that gathered by the Agency must be evaluated and considered in light of the risk information. If the Agency determines that the risks appear to outweigh the benefits, the Agency can initiate action under FIFRA Section 6(b)(1) to cancel the registration for a use, or to modify the terms and conditions of registration for the use. FIFRA Section 6(b)(2) proceedings are appropriate (among other situations) when a pesticide use appears to pose a risk of unreasonable adverse effect, contain less than 0.1 ppm TCDD.[*]

(2) Registered Uses and Production

2,4,5-T is a selective, broadleaf herbicide. It is used mainly to clear brush and hardwood on pastures, rangeland, utility rights-of-way, and in forestry.

Agency records show that 122 companies hold federal registrations and formulate 424 products; 11 companies have applied for federal registration of 21 state-registered products (EPA 1978).

In 1969, 11,626,000 pounds of 2,4,5-T acid, esters, and salts were produced in the U.S.; 12,335,000 pounds were produced in 1970. For the period 1971 through 1974, 738,907 pounds of 2,4,5-T were imported into the U.S., for a yearly average of 148,000 pounds (EPA 1978).

(3) Tolerances

There are no tolerances established for 2,4,5-T or TCDD in or on food crops. However, 40 CFR 180.302

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[*] Although 2,4,5-T manufacturers attempt to remove this contaminant, TCDD cannot be completely removed. An EPA contract laboratory has measured the TCDD content in 16 recently produced commercial samples of technical grade 2,4,5-T from five different manufacturers. The contractor reported that the TCDD content in these samples ranged from not detectable to 0.025 ppm (limit of detection 0.01 ppm) [excluding higher values that the contractor reported as doubtful] (EPA 1979a). Therefore, because TCDD is present as a low-level contaminant in commercial samples of 2,4,5-T, references in this document to "2,4,5-T" or the "pesticide product" mean 2,4,5-T that is contaminated with TCDD.

and additional information on risks or benefits would assist the Agency in making a decision on the ultimate fate of the pesticide use.

B. Background Information Relating to 2,4,5-T

(1) Chemical and Physical Characteristics

The chemical name of the herbicide 2,4,5-T is 2,4,5-trichlorophenoxyacetic acid. Its chemical formula is $C_8H_5Cl_3O_3$. The pure acid form occurs as white crystals and has a molecular weight of 255.49; its melting point is 156.6°C with a solubility in water of 278 parts per million (ppm) at 25°C. 2,4,5-T is also soluble in acetone, ethanol, ether, and alkaline solutions. The esters of 2,4,5-T are formulated to be emulsifiable in water and soluble in most oils, while its amine salts are soluble in water, but insoluble in petroleum oils (EPA 1978).

During the manufacturing process, at temperatures above 160°C, 2,4,5-T becomes contaminated with an especially toxic polychlorinated dibenzo-p-dioxin, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). TCDD occurs as a white, crystalline solid, is 99.5% decomposed at 800°C, and is soluble in acetone, benzene, dimethylsulfoxide, and methanol. It is slightly soluble in water [0.2 parts per billion (ppb)] at 25°C (EPA 1978). Current U.S. manufacturing specifications require 2,4,5-T presently being sold to does establish a tolerance of 0.05 ppm for hexachlorophene on cotton seed with a stated limitation that the technical grade fungicide shall not contain more than 0.1 ppm TCDD. The limitation does not constitute a tolerance (EPA 1978).

(4) Regulatory History

Pesticides containing 2,4,5-T have been federally registered since 1948. A summary of regulatory actions on 2,4,5-T prior to the issuance of the RPAR is given in "2,4,5-T: Position Document 1" (EPA 1978). Subsequent regulatory actions are summarized in Part I of this document.

II. REBUTTAL ANALYSIS

The 2,4,5-T RPAR notice cited two risk criteria which both 2,4,5-T and TCDD had met or exceeded. [All such risk criteria are listed in the Code of Federal Regulations, 40 CFR 162.11(a)(3).] These two risk criteria were oncogenic effects in test animals [40 CFR 162.11(a)(3)(ii)(A)] and chronic and/or delayed toxicity causing teratogenic or fetotoxic effects in test animals [40 CFR 162.11(a)(3)(ii)(B)].

A. Rebuttals Relating to the Presumption of Oncogenicity

The Agency received responses from two respondents to our request for rebuttal comments and additional information on this risk criterion. The Agency has reviewed the rebuttals submitted by the respondents and has concluded that these rebuttals do not rebut the oncogenic effects risk presumption upon which the RPAR was partially based. The four laboratory studies, cited in the RPAR notice, in which oncogenic effects were reported for test animals exposed to TCDD and/or 2,4,5-T are summarized below.

Muranyi-Kovacs et al. (1969) administered 2,4,5-T (containing <0.05 ppm TCDD) to inbred C3Hf and XVII/G mice by giving 100 mg/liter in the drinking water for two months beginning at six weeks of age, and 80 ppm in the diet during the succeeding 15 to 20 months. In C3Hf mice, 48 percent of the treated females (12/25) and 55 percent of the treated males (12/22) developed tumors, compared with control values of 21 percent (9/44) and 49 percent (21/43), respectively. In XVII/G mice, 84 percent of the treated females (16/19) and 75 percent of the treated males (15/20) developed tumors, compared with control values of 53 percent (21/40) and 78 percent (25/32), respectively.

Innes et al. (1969), under contract with the National Cancer Institute, studied the tumorigenicity of 2,4,5-T, containing possibly as much as 30 ppm TCDD, in two hybrid strains of mice, designated as "X" and "Y", after oral or subcutaneous administration of the maximum tolerated dose. Results of the studies were calculated comparing treated groups with matched and pooled controls. In the subcutaneous study, mice were given a single injection of 21.5 mg/kg of 2,4,5-T at about 18 months of age. Seventeen percent (3/18) of the treated "Y" males developed pulmonary adenomas. This incidence of pulmonary adenomas was significant relative to both control groups. In the oral study, 21.5 mg/kg of 2,4,5-T was administered daily, beginning at 7 days of age. After weaning, 60 ppm of 2,4,5-T in the diet was provided until the end of the study at about 18 months. Gross and histological examinations were made of all major organs and visible lesions; thyroid glands were not examined. There were no significant differences between treated and control groups of mice with respect to tumors at specific sites or total number of tumor-bearing animals (Memo 1979a; 1979b).

Van Miller et al. (1977) reported the results of a two-year feeding study with male Sprague-Dawley rats fed ground chow containing 0.1, 5, 50, or 500 ppt and 1, 5, 50, 500, or 1,000 ppb TCDD. Tumorigenic and toxic effects were observed in rats in the six lowest dose groups.

Dow Chemical Company (1977) reported preliminary results of a study of TCDD's chronic toxic effects in Sprague-Dawley rats fed TCDD at 0.1, 0.01, or 0.001 ug/kg body weight daily (about 2,200, 210, and 22 ppt in the diet) for two years. Dow reported "discernible increases" in the incidence of hepatocellular carcinomas of the liver and of squamous cell carcinomas of the lung, hard palate/nasal turbinates, and tongue in rats at 0.1 ug/kg. Hepatocellular nodules and alveolar hyperplasia were observed in the 0.01 ug/kg group.

(1) Carcinogenic Potency of TCDD

(a) As a Complete Carcinogen

Dow Chemical (30000/26:#16)[*/] commented that laboratory researchers for the National Cancer Institute have concluded that "TCDD is a weak carcinogen in animals." Conversely, Harris (30000/26:#2392) commented that, on the basis of work done at the University of California, TCDD is about 10 times more potent than the potent human carcinogen, aflatoxin.

Recent communication to the Agency's Carcinogen Assessment Group (CAG) from the National Cancer Institute (NCI) on its as yet incomplete study on TCDD in rats and mice indicate that TCDD

[*/] Rebuttal citations refer to accession numbers in OPP's Federal Register Section. Rebuttals are available for public inspection.

appears to be as potent as observed in the Sprague-Dawley rat study performed by the Dow Chemical Company (Memo 1979b). In citing the published abstract of the NCI study, Dow stated only part of the total thought. The entire sentence reads, "This study suggests that TCDD and HCDD are weak carcinogens given orally and are complete carcinogens when applied to the skin."**/

In addition, CAG has independently calculated the relative potency of TCDD as a carcingoen and has concluded that TCDD is a more potent carcinogen than aflatoxin. This analysis is consistent with the information given in the Harris rebuttal (Memo 1979a).

(b) As a Promoter

Dow Chemical Company (30000/26:#16) further argued that Van Miller et al. stated that their study did not prove conclusively that TCDD is a carcinogen. They suggested that TCDD was acting as a "potent promoter" of neoplastic changes, and that this led to the wide variety of tumors reported to be associated with ingestion of low dose levels in the diet.

**/ The results reported in this abstract were increased hepatic tumors among male mice and markedly increased epithelial tumors in female mice due to oral TCDD exposure. Dermal exposure resulted in skin tumors, increased in both numbers and aggression.

This rebuttal raises two issues relating to the carcinogenicity of TCDD: 1) does TCDD induce cancer development in experimental animals; and 2), if so, does TCDD produce the carcinogenic effects by acting as a co-carcinogen or promoter at low levels as Van Miller et al. implied. With regard to the first issue, the Dow Chemical Company study, as well as the Van Miller et al. study, showed that TCDD is a carcinogen in the same strain of rats (Sprague-Dawley), exposed through the same route of administration (feeding in diet), and exposed to comparable dose levels ranging from 2,200 ppt in the Dow study to 1,000 ppt in the Van Miller study.[*] In regard to the second issue of whether TCDD acts as a promoter or as a carcinogen, the Agency regards any compound which induces a carcinogenic response as a carcinogenic hazard regardless of its mechanism of action (Memo 1979a; 1979b).

(2) Lowest Effect Level of TCDD

In reporting its rat feeding study, Dow did not consider the effects seen at 210 ppt TCDD as indicative of a positive carcinogenic effect. Harris (30000/26:#2392) commented that in the Dow study, 220 ppt [sic] in the diet also appeared to induce liver tumors in female rats.

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[*] The Agency evaluation of this study indicates that it has experimental deficiencies which limit the reliability of the results at dose levels below 1,000 ppt. However, these deficiencies do not affect the positive findings observed at higher doses.

only one was reported to have been associated with a statistical increase in tumors. Dow further claimed that even this observation was non-reproducible when the same investigators gave 2,4,5-T to the same strain of mice by a different route of exposure. Moreover, as the number of studies increases, the probability of false positive results increase.

The Agency acknowledges that the Muranyi-Kovacs study is deficient in the following respects: 1) only one dose was used; 2) the animal husbandry was inadequate, as acknowledged by the authors (Memo 1979a); 3) the histology data on all animals were not available; 4) some mice were arbitrarily excluded from the calculations of tumor incidence; and 5) the authors themselves were reluctant to defend the results. For these reasons, this study cannot alone be regarded as establishing the carcinogenicity of 2,4,5-T.

However, although the Muranyi-Kovacs study did not produce tumors in single target tissues as a result of exposure to 2,4,5-T, this study did show a statistically significant excess of combined tumors in important organs in animals treated with 2,4,5-T (liver, leukemia, and other rare tumors not found in control animals). In addition, the editor and referees of the British Journal of Cancer, publisher of the study, believe that the statistical method

CAG has re-evaluated this study and now concludes that the combined incidence of hepatocellular hyperplastic nodules and hepatocellular carcinomas is statistically significant at both the 2,200 and 210 ppt level.

(3) Enzymatic Effects

Dow Chemical (30000/26:#16) commented upon EPA's statement that TCDD has possible carcinogenic potential because it is an inducer of arylhydrocarbon hydroxylase (AHH). Dow maintained that the induction of AHH by TCDD has no bearing on the carcinogenic potential of this chemical.

The Agency notes that, although the biochemical mechanism of tumor induction by TCDD is not known in detail, TCDD is known to be a potent inducer of the arylhydrocarbon hydroxylase system. Epoxidase, one component of the AHH system, is known to be involved in the metabolic activation and carcinogenicity of polycyclic aromatic hydrocarbons. Therefore the carcinogenic action of TCDD could be mediated by this enzyme system.

(4) Carcinogenicity of 2,4,5-T

Dow Chemical (30000/26:#16) claimed that the Agency's characterization of 2,4,5-T as a carcinogen was in error. According to Dow, out of a total of 10 animal studies based on chronic exposure to 2,4,5-T, than the substantive validity of the toxicological studies. The Agency has reviewed the rebuttals and additional information submitted by the registrants on the reproductive toxicity of 2,4,5-T and TCDD and has concluded that this risk criterion has not been rebutted. The studies cited in Position Document 1 are summarized below.

Fetototoxic and embryolethal effects have been reported in studies[*] using generally low-dose regimens of TCDD. For example, Neubert and Dillmann (1972) reported that resorption sites (resorbed or dead embryos) occurred in 54% (7/13) of the litters at 0.3 ug/kg per day and in 100% (3/3) of the litters at 9.0 ug/kg per day for NMRI mice, compared to 24 to 32% (23/95 and 21/65) of litters exhibiting resorptions in control animals which had not been exposed to TCDD. Sparschu et al. (1971) reported resorptions of 100% (110/110) of the fetuses in Sprague-Dawley rats exposed to 8 ug TCDD/kg per day, compared to 20% resorption (63/309) of the fetuses from the control animals. Khera and Ruddick (1973) reported 100% (77/77) resorption of fetuses at 4 ug/kg per day and 36% (56/153) at exposures of 1 ug/kg per day in Wistar rats, compared to 2 to 7% (3/152 and 10/127) in the control animals.

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[*] Except as otherwise noted, the studies on the fetotoxic and embryotoxic effects of TCDD and 2,4,5-T with TCDD involved the daily oral administration of the chemical to pregnant test animals for the period of major organogenesis during gestation (e.g., on gestation days 6 to 15).

used in the evaluation of the tumor data is valid for the data generated (Memo 1979a). For these reasons, the Agency does not accept all points in Dow's rebuttal.

Dow Chemical Company (30000/26:#16) further claimed that the (subcutaneous injection) study cited by the Agency as a basis for the presumption against 2,4,5-T was incorrectly interpreted and that no increased tumor incidence was reported by the original investigators (Innes et al. 1969).

Although animal bioassays in which 2,4,5-T, was administered to test animals yield somewhat inconclusive results, the presence of small quantities of TCDD, a potent oncogen, in commercial 2,4,5-T means that pesticide products containing 2,4,5-T also contain an oncogenic agent. The oncogenic effects reported in bioassays using 2,4,5-T as the test material may not have been as pronounced as those reported for TCDD because the test animals exposed to 2,4,5-T were exposed to lower dose levels of TCDD than the levels which produced significant carcinogenic effects in animals exposed to pure TCDD.

B. Rebuttals Relating to the Presumption of Reproductive and Fetotoxic Effects

The Agency received numerous responses to its request for rebuttal comments and additional information on this risk criterion. Most of these comments addressed the question of human exposure potential[*/], rather

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[*/] See Section II.C.

In a preliminary report of a study of the effects of TCDD on reproduction in Sprague-Dawley rats exposed to low levels for three generations, Dow Chemical Company (1977) concluded that "impairment of reproduction was clearly evident among rats ingesting 0.01 or 0.1 ug TCDD/kg per day. Significant decreases were observed in fertility, litter size, gestation survival, post-natal survival, and postnatal body weight."*/

Exposure to TCDD has also produced skeletal anomalies and injury to internal organs in the offspring of animals treated during pregnancy. Courtney and Moore reported the following incidences of cleft palate in the indicated strains exposed by subcutaneous injection to 3 ug/kg per day TCDD: 71% (5/7) in litters of C57BL/6 mice, compared to none (0/23) in the controls; 22% (2/9) in litters of DBA/2 mice, compared to none (0/23) in the controls; and 30% (3/10) of CD-1 mice, compared to none (0/9) in the controls. Neubert and Dillmann, also using 3 ug/kg per day TCDD, reported 29% (7/24) of the viable litters had fetuses with cleft palate for NMRI mice, compared to 6% (10/160) of the control litters. Smith et al. (1976) reported cleft palate in 71% (10/14) of CF-1 mouse litters at 3 ug/kg per day, compared to none (0/34) in the controls.

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*/ Dow Chemical Company has claimed that the raw data and/or results of certain of its studies are "trade secret" or "confidential." An injunction issued on April 4, 1978, in the case of Dow Chemical Co. v. Costle, Civil Action No. 76-10087, U.S. District Court for the Eastern District of Michigan (Northern Division), arguably precludes EPA from disclosing this information at the present time. Although the relevant provisions of FIFRA have since been amended to allow disclosure of data such as this [see e.g., FIFRA Sections 10(d) and 10(g)], the injunction has not yet been modified. EPA has requested the Court to modify the injunction, but until this has been done, the Agency will not publicly disclose the data from the study. The summary presented in the text of this Position Document does not, in EPA's opinion, constitute disclosure of the allegedly "trade secret" data submitted by Dow and would not cause any harm to Dow's legitimate competitive interests. The data from the study may be made available to any party in a cancellation proceeding under an appropriate protective arrangement.

In exposures of shorter duration, Moore et al. (1973) reported cleft palate in 86% (12/14) of C57BL/6 mouse litters exposed on days 10-13 of gestation to 3 ug/kg per day, compared to none (0/27) in the control litters. Neubert and Dillmann (1972) reported cleft palate in 71% (10/14) of litters of NMRI mice exposed to a single 45 ug/kg dose on gestation day 11, compared to 6% (6/95) of litters in the controls.

Smith et al. (1976) reported 28% (4/14) of litters with kidney anomalies at 3 ug/kg per day TCDD in CF-1 mice, compared to none (0/34) in the controls. Moore et al. (1973) reported 100% (14/14) of litters with kidney anomalies in C57BL/6 mice exposed to 3 ug/kg per day on gestation days 10-13, compared to none (0/27) in the control litters. Courtney and Moore (1971) administered TCDD subcutaneously to CD-1 mice on gestation days 6-15 and reported kidney anomalies in 100% (10/10) of the litters at 3 ug/kg per day, compared to 33% (3/9) in the controls, and 67% (4/6) litters with abnormal kidneys in the CD rat at 0.5 ug/kg per day, compared to none (0/9) in the control litters. Sparschu et al. (1971) reported hemorrhages or lesions of the intestine of 36% (36/99) of the examined fetuses of Sprague-Dawley rats exposed to 0.5 ug/kg, compared to none (0/246) in the control fetuses.

Cleft palate, high incidences of fetal mortality, reduced fetal weight, and other indicators of injury to the developing fetus have been reported in several studies in which test animals were exposed to 2,4,5-T contaminated with varying levels of dioxin. Some of these effects have been reported in test rodents at maternal doses as low as 20 mg/kg 2,4,5-T containing 0.5 ppm TCDD. For example, Neubert and Dillmann (1972) studied the effects of 2,4,5-T contaminated with dioxin in NMRI mice. Using 2,4,5-T with 0.05 ppm TCDD, these investigators reported resorptions in 57% of the litters and cleft palate in 71% of the litters at 60 mg 2,4,5-T/kg, compared to 24 to 32% resorptions and 6% cleft palate in the controls.

Similarly, Courtney and Moore (1971) reported that oral exposure of CD rats to 80 mg/kg per day 2,4,5-T containing 0.5 ppm TCDD led to 52% fetal mortality per litter, compared to 3.4% in the controls. At this dose, kidney anomalies were observed in 50% of the litters, compared to none in the controls, but none of the fetuses had cleft palate at any dose. However, subcutaneous injection of 100 mg/kg 2,4,5-T containing 0.05 ppm TCDD led to cleft palate in 40% of the litters of CD-1 mice, compared to none in the controls.

Collins and Williams (1971) studied the effects of 2,4,5-T containing various amounts of dioxin on the reproduction in the Syrian hamster. At 20 mg/kg 2,4,5-T (containing 0.5 ppm TCDD), there were significant decreases in fetal weight and viability. The same type of effects were seen with 2,4,5-T containing less than 0.1 ppm TCDD at 80 mg/kg. Exposure to higher doses of this 2,4,5-T resulted in an increased incidence of fetal anomalies, such as exencephaly, eye abnormalities, delayed head ossification, and hind limb deformities.

(1) Nature of Fetotoxic Effects

Several commenters attempted to rebut the fetotoxic risk criterion by arguing that 2,4,5-T and/or TCDD are not teratogenic because the abnormal effects are observed only in sensitive species of test animals and are generally types other than gross anatomical defects. Examples of specific arguments are: (1) the observed kidney anomalies are really retardation of normal development and not "true" terata [Dow (30000/26/:#16)]; and (2) TCDD is more of a toxicant than a teratogen, usually causing death of the fetus rather than abnormalities [CAST (30000/26:#2297)].

Rebuttal arguments of this type are not persuasive when considered in terms of either scientific or legal criteria. Although there may be many differences between, for example, animals born with anatomical defects and stillborn or size-retarded animals, the essential fact is that both groups of animals have been injured and/or are abnormal. Thus, in terms of human health consequences, the distinction that Dow makes is a distinction without a difference. Moreover, because FIFRA charges the Agency with protecting the environment from any unreasonable adverse effects, the Agency's ability to regulate is not limited only to certain types of adverse effects, particularly when, as here, differences between certain effects relate to mechanism of origin, not to health consequences.

The same reasoning applies to the distinction between growth retardation and "true" teratogenesis. For regulatory purposes, it is not relevant whether the observed anomalies are retardation or "true" teratogenic effects. An infant born with retarded mental or physical development is clearly disadvantaged, and possibly subject to increased risk during any "catch-up" period, even though the handicap may ultimately be overcome.

(2) Maternal Toxicity

Several commenters argued that the effects observed on the fetus are the secondary result of maternal toxicity, rather than a direct effect on the fetus. "When gestating animals are poisoned by massive doses of any substance, there are usually adverse effects on the developing offspring" [CAST (30000/26:#2297)].

This again is primarily a mechanism of action argument. In addition, arguments based on maternal toxicity find little support in the experimental data. Fetal effects have routinely been observed in mammalian species at doses where the mothers appear perfectly normal. [See, for example, the Schantz et al. (1979) monkey study at 50 ppt in Section III.A.(1)]. As for the use of "massive doses," adverse fetal effects have repeatedly been reported at low dose levels where no adverse maternal effects have been observed. A simple comparison of reproductive effect levels with LD_{50} values demonstrates the weakness of this argument (even though reproductive studies involve low-level, repeated daily doses and acute toxicity studies are usually carried out with higher dose levels administered once). For example, reproductive effects have been observed in the rat at doses as low as 1/40,000 of the LD_{50} for adult animals.

(3) No-Effect Levels

Dow Chemical Company (30000/26:#16) argued that there are ample margins of safety for women of child-bearing age between potential exposure and no-effect levels. As the bases for calculating these margins of safety, Dow used values from the 2,4,5-T RPAR.

The Agency cannot accept the margins of safety suggested by Dow because studies by Dow and others which became available to the Agency after issuance of the RPAR clearly show that effects are observed in test animals at levels lower than those reported in the RPAR. For example, in a new Dow reproduction study using rats (Dow Chemical Co. 1978) fetotoxic and teratogenic effects were reported at 0.001 ug/kg per day, the lowest dose tested in any species to date. Because effects are observed at the lowest dose levels to which the test animals were exposed, it is possible that adverse effects occur at lower, as yet untested, dose levels. Finally, because the lowest levels at which effects may occur are unknown, and because effects nevertheless are observed at low levels of exposure which approach levels to which humans may be exposed, there may be no adequate margin of safety. Therefore, because of the known opportunities for human exposure, and the absence of an established level at which there are no adverse effects, neither Dow nor the Agency can reliably determine whether or not there is an adequate margin of safety.

(4) Species Specific Teratogenic Effects

Dow (30000/26:#16) states that the subject chemicals are teratogenic only "in certain strains of mice which are genetically predisposed to the development of cleft palate" and that "[t]he effects seen in other species and other strains of mice are either embryotoxic or fetotoxic, not teratogenic effects."

The Agency does not agree with Dow's contention that the teratogenicity of 2,4,5-T and/or TCDD has been observed only as cleft palate in certain susceptible strains of mice. Other anomalies such as dilated renal pelvis and delayed ossification have been seen in rats, and palate abnormalities have been seen in monkeys [see Section III.A.(1)]. Other types of teratogenic effects have been observed in studies using 2,4,5-T and/or TCDD, most notably kidney anomalies.

Use of a susceptible strain has the advantage of making the experimental system more sensitive. In addition, any baseline effects due to the particular sensitivities of the test strain should be nullified through the customary use of adequate controls. Finally, in making regulatory decisions, the Agency has traditionally used results obtained in the most sensitive species as the basis for evaluating the potential risk to humans from exposure to a given substance. This is because of the very real possibility that humans too may be "genetically predisposed" to a given teratogenic effect.

(5) Teratogenic Potency of TCDD

A report, "The Phenoxy Herbicides," submitted by the Council for Agricultural Science and Technology (CAST) [30000/26:#2297] concluded that TCDD should be classed as a weak teratogen because of the narrow range of dosage between the no-effect level on the fetus and the lethal effect on the mother.

The Agency disagrees with both premises in this rebuttal. First, in marked contrast to CAST's position, many scientists interpret the data showing that TCDD produces many different birth defects in several different species at very low dose levels as indicating that TCDD is one of the most potent teratogens known. Moreover, because of the many and varied uses of TCDD-containing herbicides, significant segments of the population may be exposed to TCDD. This combination of high toxicity and significant exposure clearly results in signficant risk potential for persons who are exposed to TCDD-containing herbicides. Further, even though TCDD has lower teratogenic activity in some animal tests, the risk potential for humans appears to be significant because the uses of the pesticide result in substantial exposure to some population groups.

Second, CAST's reliance on a no-effect level as the basis for its position is misplaced because significant adverse effects have been observed in the offspring of animals from the lowest-dose groups tested. More specifically, the fetal effect level for TCDD in rats is 0.001 ug/kg per day, which is over 40,000 times lower than the LD_{50} (0.045 mg/kg) for adult female rats. The difference between 0.001 ug/kg per day and 45 ug/kg clearly is not a narrow range.

(6) Fetotoxicity in Nonhuman Primates

Dow (30000/26:#16) cited two negative studies in rhesus monkeys (Wilson 1971; Dougherty et al. 1976) to demonstrate that 2,4,5-T lacked teratogenic potential in subhuman primates. McNulty (30000/26:#915) submitted data indicating that low maternal exposure to TCDD during pregnancy resulted in an increased incidence of spontaneous abortions. Leng (30000/26:#16E), of Dow Chemical Company, questioned

McNulty's results on the basis of whether maternal exposure was really as low as it appeared.

The studies cited by Dow were designed to focus primarily on teratogenic effects. In Dougherty, pregnant monkeys were administered 2,4,5-T, containing 0.05 ppm TCDD, "at dose levels approximating human exposure." No evidence of teratogenesis was observed. The authors concluded that 2,4,5-T was not teratogenic at the levels tested. However, the negative results on teratogenicity were for a relatively narrow dose range and did not cover early embryogenesis. Moreover, a close analysis of the study indicates that there may be other evidence of fetotoxicity in the form of increased abortions. In light of the TCDD studies cited above, the apparent doubling of the abortion rate observed in this study cannot be ruled out as a possible effect. Sufficient experimental details regarding the second "study" (Wilson 1971) are not available in the cited reference to allow for an adequate assessment of the study.[*] However, evidence of abortion, lowered birth weight, and incomplete ossification were indicated. In analyzing effects on nonhuman primates, Dow chose to ignore available information which demonstrates fetotoxic effects in monkeys at doses of TCDD where no maternal toxicity was observed prior to the abortion [see Section III.A.(1)].

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[*] For example, information regarding dioxin contamination of the 2,4,5-T, method of dosing, and methods of analysis were not included.

Leng challenged the results observed by McNulty by arguing that the equivalent dietary dose reported by McNulty was lower than the actual dose used. McNulty administered a total of 1 ug/kg in 10 ml acetone-corn oil in nine doses, three times a week, over a three-week period. This is about 0.1 ug/kg per dose, or 0.05 ug/kg per day, if the dosing had been daily. Using the standard dietary consumption figure for the rhesus monkey, this represents a dose of 1,000 ppt in the diet for the 20 days. Leng argued that the correct figure should be 75,000 ppt, and that any extrapolation to human dietary consumption should be based on this figure. To arrive at this figure, Leng divided the total weight of the dose by the weight of the oil (based on density). In short, 75,000 ppt represents the relationship of the TCDD to the oil. This is not the common meaning given to "ppt" when it is used to express a dose, and certainly does not represent a dietary equivalent.

(7) Combined Effects of 2,4,5-T and TCDD

Dow Chemical Company (30000/26:#16) argued that the level of TCDD in 2,4,5-T must exceed current specifications, and be greater than 1 ppm, before the "toxicity" of TCDD becomes detectable. According to Dow, animal studies have indicated that this amount of TCDD does not enhance or potentiate the toxic effect of 2,4,5-T.

In making this assertion, Dow has again apparently made a distinction between fetotoxicity and teratogenicity which, for purposes of regulation, the Agency does not recognize. The lack of teratogenic effects will not negate other fetotoxic effects observed under the same experimental conditions. For example, in one of the studies cited and conducted by Dow, there was no increase in teratogenic effects; however, there was a significant increase in fetal loss at the lowest dose of TCDD (0.01 ug/kg per day) combined with 2,4,5-T, when compared to the effect of 2,4,5-T alone.*/ Like teratogenic effects, this increased fetal loss is an indicator of injury to the fetus.

(8) Agency Analysis

Another Dow rebuttal argument (30000/26:#16) was that the Working Group appeared to give all studies cited in the RPAR notice equal weight and validity without regard to study quality. As an example, Dow cited the Agency's use of a study in which dose levels were given in millimoles per unit body weight, rather than in weight per unit body weight. This use of an uncommon dose unit caused Dow to argue that the study's results could not be readily compared with other studies.

The Agency cannot accept this argument. A thorough reading of the RPAR notice will show that whenever possible, confounding factors, such as maternal toxicity, were observed in a study, the Working Group noted them in its reporting of that study. Any omissions were by inadvertence, rather than design. Even if Dow's argument were sound, and several of the studies could be invalidated or given lesser weight, one still could not ignore the overwhelming consensus of the many studies in this area: TCDD and/or 2,4,5-T contaminated with TCDD are clearly fetotoxic and teratogenic agents.

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*/ Dow has also claimed that the raw data and/or results of this study are confidential. See previous footnote on this subject.

As to Dow's example, the Agency agrees that millimoles per unit body weight is an uncommon expression of dose. However, the simple multiplication of the millimoles by the molecular weight of the compound will yield the more familiar dose expression of weight per unit of body weight.

C. Rebuttals Relating to Exposure

Most of the substantive rebuttals to the 2,4,5-T RPAR addressed the question of potential human exposure to 2,4,5-T and/or TCDD. The bulk of these comments challenged the exposure estimates included in Position Document 1; others, however, offered constructive suggestions for improving the Agency's exposure analysis without addressing any specific point in the RPAR.

The Agency's exposure estimates are designed to approximate actual exposure. The estimates are based on relevant data and, when such data are not available, on assumptions relating to probable exposure. The accuracy of these estimates depends in part on the bases of the assumptions. The more empirical data supporting the assumption, the more reliable the exposure estimate.

When Position Document 1 was written, very little empirical data were available on 2,4,5-T human exposure levels. Since then, partially in response to the RPAR, additional information has become available. The Agency has re-examined its exposure analysis in light of this new data and has concluded that for some use situations, the estimates in the Position Document may have been higher or lower than actual exposure would be.

Because toxicological data which Dow Chemical Company presented to the Agency after issuance of the RPAR indicate that there are no no-effect exposure levels for the fetotoxic and teratogenic effects associated with TCDD, and consequently for 2,4,5-T containing TCDD, the quantitative exposure estimates for 2,4,5-T and TCDD upon which the RPAR was based have little value beyond suggesting the potential for exposure. The discussion below summarizes the Agency's original estimates and the rebuttals to these estimates.

In Position Document 1, the 2,4,5-T Working Group set forth several estimates for the oral, dermal, inhalation, and cumulative exposures to 2,4,5-T and TCDD for a woman weighing 60 kg, in a variety of situations. Upon reviewing these estimates, the Working Group recommended that the Agency issue an RPAR for all pesticide products containing 2,4,5-T.

Oral Exposure: After determining the average daily consumption of beef and milk contaminated with 2,4,5-T, the Working Group calculated that the cumulative oral exposure to 2,4,5-T could be 0.0007 mg/kg per day. Because information on TCDD residues in beef was sparse, the Agency did not calculate the oral exposure to TCDD through the ingestion of contaminated beef or milk.

Dermal Exposure: Extrapolating from both dermal exposure data for fenthion and information on the concentration and dilution rates for 2,4,5-T, the Working Group estimated that an applicator using a backpack sprayer would be exposed to 6.8 mg/kg of 2,4,5-T and 0.0007 ug/kg of TCDD per day. The Agency also calculated that the dermal exposure to 2,4,5-T and TCDD for a spray applicator, using tractor-mounted, low-boom spray equipment, would be 1.8 mg/kg and 0.00018 ug/kg per day, respectively. These estimates were based, in part, on exposure studies using similar equipment, but a different herbicide, together with the concentration and dilution rates for 2,4,5-T. For the exposed population directly beneath the spray plane, the Working Group determined that the daily dermal exposure estimates would be 0.051 mg/kg for 2,4,5-T and 5×10^{-6} ug/kg for TCDD.

Inhalation Exposure: EPA also estimated that unprotected persons directly beneath a spray plane would inhale 0.026 mg/kg of 2,4,5-T and 2 X 10^{-6} ug/kg of TCDD for each day of application. Due to the fact that no studies on 2,4,5-T inhalation exposure were available, the Agency based these estimates, in part, on several studies which provided similar exposure data for malathion.

Cumulative Exposure: In addition to providing oral, dermal, and inhalation exposure estimates, the Agency also calculated cumulative levels of exposure to 2,4,5-T and TCDD for three different situations. The Working Group supplied these estimates because of the possibility of a single individual being exposed through two or more of the above routes. The Agency estimated that cumulative exposure for a spray applicator using a backpack sprayer would be 7 mg/kg for 2,4,5-T and 0.0007 ug/kg for TCDD, based on an average concentration of 0.1 ppm of TCDD (EPA 1978). For those applicators using tractor-mounted, low-boom spray equipment, cumulative exposure would consist of 1.85 mg/kg of 2,4,5-T and 0.00018 ug/kg of TCDD (EPA 1978). Finally, the Working Group determined that those directly beneath the path of a spray plane would be subject to a cumulative exposure of 0.0777 mg/kg of 2,4,5-T and 7 X 10^{-6} ug/kg of TCDD (EPA 1978).

(1) Basic Assumptions

(a) Level of TCDD Contamination

Laverty Sprayers, Inc. (30000/26:#75) commented that although significant amounts of dioxin have contaminated

2,4,5-T in the past, manufacturers have shown that they can now drastically reduce the dioxin levels. Laverty asserts that 0.1 ppm therefore does not represent the level of TCDD contamination on the present product, and urges that the Agency consider the "new" 2,4,5-T to a greater degree than the obsolete product.

The Agency acknowledges that manufacturers can make 2,4,5-T with less than 0.1 ppm dioxin contaminant.*/ However, since the current manufacturing specifications permit up to 0.1 ppm TCDD in 2,4,5-T, it was appropriate for the Working Group to use this level of contamination in their calculations.

(b) Worst Case Assumptions

William M. Upholt (30000/26:#50) and the National Cattlemen's Association (30000/26:#77C) questioned the Agency's exclusive use of "worst case" assumptions, rather than "average case" assumptions.

Ideally, exposure estimates provide information regarding the exposure encountered by all segments of the population. Unfortunately, data is not always available to make these estimates. Hence, "worst case" estimates are

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*/ Recent Agency analysis of 16 commercial samples of 2,4,5-T found that the TCDD content in these samples ranged from not detectable to 0.025 ppm (limit of detection: 0.01 ppm) [excluding higher values that the contractor reported as doubtful].

used as a means to assess the risk to the population segment receiving the greatest exposure and therefore, the greatest risk. Considerations for other elements of the population can be made from these determinations.

The Agency's use of "worst case" assumptions is consistent with a conservative approach to assessing the potential risks of human exposure to toxic substances. This approach takes into consideration the risks involved for persons who have above average exposure, as well as those with "average" exposure. Because every average is the mean of some higher and some lower values, "average case" assumptions would address only the average and below, and would preclude the Agency from identifying other populations which may be at greater than average risk.

(c) Female as a Model

Detroit Edison Company (30000/26:#210) and The National Cattlemen's Association (30000/26:#77C) objected to the Agency's use of a female model for the calculations. These commenters asserted that this approach, "*a priori*," would result in excessive exposure estimates (in mg/kg) for the same absolute amount of exposure, because of a woman's smaller weight. The Pacific Legal Foundation (30000/26:1015) argued that women applicators are more appropriately the concern of the Occupational Safety and Health Administration (OSHA), and that EPA should, at most, require labels which warn of the possible harm to pregnant applicators.

In developing the Position Document, the Agency found that major risks of exposure to 2,4,5-T and/or TCDD were fetotoxic and teratogenic effects. Since these reproductive effects apply only to the developing fetus, the exposure of possibly pregnant women was of necessity considered. This led naturally to the use of a woman's weight in the calculations. However, even if the weight of a man (70 kg) had been used instead, the exposure estimate would have changed only by about 17%.

The argument made by the Pacific Legal Foundation is based on an incorrect view of the law. EPA has an obligation under FIFRA to protect applicators of pesticides from unreasonable adverse effects.

(d) Protective Clothing and Devices

Several respondents argued that the Agency did not take into consideration the use of protective clothing and devices when calculating potential exposure, and that use of such protective items would reduce the total amount of exposure, particularly by dermal routes, by an estimated 10 to 20%.

The Agency based its initial exposure estimates and related risk estimates on the potential for exposure under conditions of ordinary, unregulated use. This approach is sound because existing regulations requiring protective clothing and devices are not universally applicable to all 2,4,5-T users and uses. For example, such regulations might apply to persons in some occupations in some states, but not to the same workers in other states nor to bystanders not subject to the regulations. Further, even when such regulations are in effect, some users and applicators may ignore the regulations and label warnings. Thus, in order to assess the exposure potential under ordinary use conditions, the Agency considers probable and worst-case exposure situations, rather than well-regulated conditions. This approach requires the Agency to make conventional allowances for clothing.

(2) Specific Calculations

(a) Oral Exposure

(i) Urinary Excretion of 2,4,5-T

The National Cattlemen's Association (30000/26: #77C) argued that, in calculating oral exposure, the Agency had ignored the fact that 95% of ingested 2,4,5-T is eliminated in the urine within 96 hours.

The respondent is apparently basing the comment on the work of Sauerhoff et al. (1976), but this is unclear from the rebuttal. The Agency agrees that 2,4,5-T is relatively rapidly excreted in the urine. However, even 96 hours (4 days) represents a significant period of exposure for adverse effects during a susceptible period for the developing fetus, or for the initiation of a carcinogenic response. In addition, this clearance period of 96 hours is for 2,4,5-T. It has no relevance to the retention of TCDD in the body.

(ii) FDA Market Basket Survey

The University of California Cooperative Extension (30000/26:#1299A) commented that the FDA "Market Basket Survey" has failed to show 2,4,5-T present in any food composite at or above 0.02 ppm, and that a specific search for TCDD in milk with the best existing method was also negative.

The Agency considers the "Market Basket Survey" a reasonable indicator of the dietary intake of the population as a whole. However, the survey results are not to be taken as absolutes. The occasional sample or batch of food with a high 2,4,5-T or TCDD content could be missed in the random sampling. Foodstuffs which do not pass through the market before being consumed are not considered. Also, and this is particularly relevant to TCDD exposure, the analytical methodology used in the survey may not be sophisticated enough to detect very small quantities - quantities, however, which may be sufficient to cause adverse effects. Because these adverse effects (e.g., teratogenic effects) could conceivably result from a single exposure, the Agency cannot ignore the possibility that there are residues in food which escape detection in the "Market Basket Survey." Moreover, even non-detectable 2,4,5-T and/or TCDD residues in food could contribute to the total body burden of the exposed population, and could contribute to unacceptable levels of risk from cumulative exposure.

(iii) Beef Residues

The University of California Cooperative Extension (30000/26:#1299A) argued that the estimate for 2,4,5-T provided in Position Document 1 was based on a single highly artificial animal feeding experiment, and was therefore meaningless. In addition, Dow Chemical Company (30000/26:#16B) and the National Cattlemen's Association (NCA) [30000/26:#77C] argued that if label restrictions were followed, the withdrawal periods for meat and dairy cattle would reduce the possibility of significant residues.

Reliable data from a feeding study using high dose levels may be scaled down to reasonable levels of exposure which might approximate the maximum oral intake likely for some individuals from dietary sources. As explained above, the Agency's exposure estimates are often "worst case" assumptions designed to assure that the Agency considers the exposure potential for highly exposed populations.

Moreover, Position Document 1 did not include an estimate for possible dietary intake of TCDD as a result of consumption of beef grazed on 2,4,5-T treated pastures or rangelands. However, after reviewing studies on persistence of TCDD in cattle, an EPA contractor has concluded:

"There is substantial evidence that TCDD is taken up by cattle feeding on treated pasture or rangeland and is stored in their fat at levels in the low parts per trillion range."*/

This conclusion was based on residue studies by Dow and others, and monitoring studies performed as part of the Dioxin Implementation Plan which showed measurable amounts of TCDD in samples of beef, beef fat, milk, and cream. The levels of residues present also generally indicated bioaccumulation.**/ The serious implications of these results cannot be ignored. They represent a very real potential hazard for people with "normal" dietary habits, and a serious threat to those with specialized eating habits, such as heavy meat consumers, and young children whose diet contains a high proportion of milk.

(iv) Milk Residues

The Commonwealth of Virginia, Division of Forestry (30000/26:#1239) commented that it is unreasonable to assume that milk from deliberately contaminated cattle would be available for human consumption without a withdrawal period. According to Virginia, if cattle were exposed just before marketing, the normal period of shipping and marketing would exceed the withdrawal period cited.

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*/ The summary concludes, "There is less conclusive, but at least suggestive, evidence that TCDD is also present in rice and in fish from treated rice fields at low parts per trillion levels. The potential for human exposure via wild game from treated areas cannot be assessed with the evidence available" (Clement Assoc. Inc. 1979).

**/ Although similar studies have not been performed on humans for ethical reasons, bioaccumulation in other mammalian species should be taken as an indicator that bioaccumulation is also possible in humans.

The Agency acknowledges that milk from "deliberately contaminated cattle" probably would not be used; however, use of milk from accidentally and/or unknowingly contaminated cattle is a possibility, and there could be residues in the milk in such cases.

(b) Dermal Exposure

(i) Nature of Exposure

The National Cattlemen's Association (30000/26: #77C) and the University of California Cooperative Extension (30000/26:#1299A) argued that there would be no exposed population under a spray plane, except in an unforeseeable accident.

In order to get direct exposure from an application by a spray plane, one need not be directly under the plane. The Agency's calculations for this type of exposure were developed using data from Caplan et al. (1956). Samples were taken from subjects working in unprotected areas which had been sprayed with malathion in oil. These subjects were not necessarily directly under the spray plane. The exposure was due to spray particles settling on the subjects. The spray residue was collected on pads placed on various parts of the body. The exposure was calculated from results of the analysis of these pads and the known surface areas of exposed skin areas. For these calculations, it was assumed that the subjects were dressed in long trousers, short-sleeved shirts with open collars, and without hats. If subjects were dressed in more scanty attire, considerably more exposure would have resulted.

In addition, information developed since the issuance of the RPAR clearly indicates that direct exposure to spray from aerial application, due to drift beyond the designated treatment area, occurs in many use areas. This situation necessitated a more broad definition of "exposed population," one which includes non-worker groups. These groups are of particular concern because their exposure is totally involuntary and unprepared-for (i.e., no safety precautions taken, as with some workers, to prevent or minimize exposure).

(ii) Rate of Dermal Absorption

The University of California Cooperative Extension (30000/26:#1299A) and Indiana State Chemist and Seed Commissioner, Dept. of Biochemistry, Purdue Univ. (30000/26:#265) challenged the Agency's use of 10% of dose as the rate of dermal absorption. California commented that although skin absorption for 2,4,5-T has not been determined 2,4-D absorption is 5.8%. Malathion is 6.8%, and ethion is 3.3.%.

The Agency acknowledges that it may be more appropriate to use the absorption rate of 5.8% for 2,4-D determined by

Maibach and Feldman (1974) since one would expect the absorption rate to be much like 2,4,5-T. It should be remembered, however, that that absorption rate was based on a five-day urinary excretion of radioactivity. Consequently, the 5.8% is a minimal value for 2,4-D. In addition to the values for malathion and ethion, Maibach and Feldman also gave absorption values for other compounds. One, carbaryl, was as high as 73.9%. Diquat at 0.3% and ethion at 3.3% are the only pesticides with absorptions below 2,4-D. Thus, although the 10% value may be too high, it may also be too low.

(iii) Duration of Dermal Exposure

Several respondents challenged the Agency's estimate of duration of dermal exposure as too long because the Agency assumed that exposure would be for a full working day. Respondents argued that exposure time is more appropriately equated with spraying time.

Evidence to support the respondents' view was not provided in their submissions. The Agency feels that as a starting point in estimating dermal exposure, the time the skin is exposed to spray could be roughly equated to spraying time, including additional increments of direct spray exposure time assuming that some applicators make multiple applications each day. In addition, even after actual direct spraying, deposited spray may remain on the applicators' skin and continue to be absorbed throughout the entire working day, or part of it until the worker washes deposited spray from the skin. Further, dermal exposure from and through clothing is possible during the spray operation and afterward until the applicator removes contaminated clothing.

(c) Inhalation Exposure

Dow Chemical Company (30000/26:#16), the American Paper Institute and National Forest Products Association (30000/26:#1023) challenged the Agency's estimate of inhalation exposure on the basis of the type of spray used in 2,4,5-T application. They argued that inhalation exposure would be negligible because a very coarse spray or microfoil is used.

The Agency agrees that coarse sprays will present less of an inhalation hazard than a fine spray, and that under usual conditions of usage, 2,4,5-T is applied as a coarse spray. Therefore, inhalation exposure may be negligible when 2,4,5-T is applied as a coarse spray, particularly when compared to dermal exposure under the same conditions.

(d) Application Procedures

Numerous respondents challenged the Agency's exposure estimates because of differences in application procedures. They argued that normal application practices would significantly reduce the levels of exposure cited in Position Document 1. Among the conditions suggested by the respondents were (1) lower application rates; (2) differences in application techniques (e.g., backpack basal application, where the spray is directed toward the lower stem and root collar); (3) reduced flying and application times; and (4) differences in application techniques (e.g., use of large-nozzle, low-pressure sprayers, which results in less fine spray or aerosols).

The Agency acknowledges that each of these application procedures can reduce the amount of exposure. However, none of them would eliminate exposure completely, and the respondents do not argue that no exposure potential would exist under the changed conditions. Therefore, because the Agency has concluded that any exposure to TCDD and/or 2,4,5-T contaminated with TCDD poses a significant risk to humans, these arguments are not sufficient to rebut the risk criteria.

(e) API/NFPA/Dow Study

The American Paper Institute (API), National Forest Products Association (NFPA), and Dow Chemical Company have prepared and submitted calculations of exposure and dose levels which were designed to reflect the formulations and procedures actually used in forest applications of 2,4,5-T. These calculations were based on (1) measurements taken during routine applications of 2,4,5-T, (2) extrapolations from urinary excretion levels to dose levels, and (3) interviews with professional foresters with field experience in application of 2,4,5-T. The values calculated by Dow from the API/NFPA study ranged from 0.002 mg/kg (not detectable to 0.01) for flagmen to 0.07 (0.01 to 0.16) for mixers. Backpack sprayers averaged 0.06 mg/kg (0.02 to 0.13).

The Agency applauds the initiative taken by these respondents in the development of much needed exposure information. Based in part on this study, the Agency has reassessed its own exposure estimates published in Position Document 1, and concluded that lower estimates probably more accurately reflect normal working conditions. Because of the similarities in application rates and procedures among the many uses of 2,4,5-T, the information developed in this study is applicable to uses other than forestry uses. However, it should be emphasized that this is one study, dealing with one set of conditions. Therefore, it may not accurately reflect potential exposure under all possible circumstances.

(3) Alternative Methods of Estimating Exposure

The Agency received a number of comments which made constructive suggestions concerning the improvement of the Agency's exposure estimate analysis. These comments, however, did not specifically challenge the exposure estimates set forth in Position Document 1. EPA appreciates the submission of these comments, some of which have assisted the Agency in the development of its more recent exposure analyses.

The Indiana State Chemist and Seed Commissioner, Dept. of Biochemistry, Purdue Univ. (30000/26:#265) stated that the Agency should have used data on the blood level of 2,4,5-T after exposure, in order to calculate levels of exposure. The Agency recognizes that information on blood levels of 2,4,5-T after exposure would be useful in determining actual exposure levels. However, there is currently an insufficient amount of valid data concerning 2,4,5-T blood levels.

William M. Upholt (30000/26:#40) suggested that the Agency should have estimated the levels of lifetime exposure to 2,4,5-T and/or TCDD for those human subjects with appreciable exposure to those chemicals. The Agency believes that this suggestion could be useful, particularly in the case of TCDD, which may have a slow metabolic turn-over rate and consequently may accumulate in human tissue.

The Environmental Defense Fund (EDF) [30000/26:#1021] stated that the continued use of 2,4,5-T is unacceptable because of the possible cumulative effects of exposure to low levels of TCDD from multiple sources. EDF suggested that because exposure to TCDD could be caused by a variety of sources, the Agency should have taken these sources into account when estimating the level of exposure to TCDD. The Agency recognizes that the environment contains multiple sources for possible human exposure to TCDD. However, for the purpose of regulating 2,4,5-T, it is important to establish potential exposure to TCDD resulting from the use of 2,4,5-T. The omission of other possible sources of TCDD exposure in the 2,4,5-T Position Document does not mean that the Agency is not aware of, and concerned about, these other sources.

EDF also suggested that the Agency record be kept open to include the results of both the EPA human milk monitoring study and similar studies which have not yet been completed. The Agency will make public the results of any monitoring study and include them in the 2,4,5-T record, whenever such studies are completed.

III. RISK ANALYSIS

There are two key components to the assessment of any chemical-related risk: (1) assessment of the toxicological properties of the chemical, and (2) assessment of exposure to the chemical. The risk assessment itself is a summation of the conclusions in each of these areas. Each component has a key bearing on the conclusion. For example, a highly toxic chemical may pose low risks if exposure is low; conversely a compound of low to moderate toxicity may pose high risks if exposure is high. In the present instance, TCDD is an extremely toxic chemical, whereas purified 2,4,5-T appears to be less toxic. However, because TCDD invariably contaminates commercial samples of 2,4,5-T, the use of, and exposure to, products containing these chemicals appear to present risks to human health. This section of the Position Document presents the data and information on toxic effects, and the relation between pesticide use and exposure which indicate that the uses of 2,4,5-T appear to pose risks to human health.

A. Toxicity in Test Animals

The studies upon which the RPAR was based are summarized with relevant rebuttal comments in Section

II of this document. The data in these studies are largely unrebutted. In addition, new data relating to the risk potential of 2,4,5-T and TCDD has come to the Agency's attention after issuance of the RPAR. These new data are summarized below.

(1) Adverse Reproductive Effects

Dow Chemical Company has recently completed the study of the effects of TCDD on reproduction in Sprague-Dawley rats exposed to low dose-levels of this chemical for three generations.*/ Dow concluded that "impairment of repoduction was clearly evident among rats ingesting 0.01 or 0.1 ug TCDD/kg per day. Significant decreases were observed in fertility, litter size, gestation survival, post-natal survival, and postnatal body weight." In addition, exposure to 0.001 ug TCDD/kg per day (the lowest level tested in this study) resulted in statistically significant increases in the percentage of pups dead at birth and/or dying before the end of three weeks of life, and in the incidence of dilated renal pelvises in some generations.

Recent reproductive studies in rhesus monkeys indicate that maternal exposure to TCDD results in an increased incidence of early spontaneous abortions and reproductive difficulties. The significance of these results in nonhuman primates should not be underestimated because of the close similarities between the reproductive systems of humans and monkeys. Long-term exposure to even minute quantities of TCDD resulted in a marked increase in spontaenous abortions in the first third of the gestational period, even where there was no evidence of maternal toxicity by clinical observation or biomedical testing. Monkeys exposed to 50 ppt TCDD (2.5 ng/kg per day) before and during pregnancy had a total fetal loss of 67% (50% by abortion and 17% as stillbirth) and fertility rate of 75%, compared with 0% and 100% in the controls. Attempts to re-breed one of the aborters resulted in an additional early abortion (Schantz et al. 1979; Memo 1979c; 1979d). When animals were treated with a higher dose, the fertility rate dropped to 25%, with one of the two gravid animals aborting in the first third of gestation. Irregularities in menstrual cycles, anovulation, and reduction in the reproductive hormones, progesterone and estrogen, were among the toxic effects seen at the higher dose. The investigators concluded that the reproductive abnormalities were most probably the result of hormone imbalance, and were apparently the result of the TCDD treatment, rather than general toxicity, because the hormonal alterations were observed before the animals became obviously ill (Allen et al. 1977; Barsotti et al. 1979).

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*/ Dow has also claimed that the results of this study are confidential.

Early abortions have also been observed in monkeys where exposure has only been for a short period of the pregnancy. An accumulated dose of 1 ug/kg (1,000 ppt) of TCDD over a three-week period resulted in a 75% abortion rate, compared with 0% in the controls. All abortions in the treated animals were during the first third of the gestational period, and the only evidence of maternal toxicity was slight chloracne in one animal, observed months later. The viable offspring produced at this dose had abnormal palate development, and three of the four at a lower dose had debatable abnormal development in the same orofacial region (Letter 1979).

The National Center for Toxicological Research (NCTR) has recently published the results of a teratological study on 2,4,5-T, using over 10,000 pregnant mice and multiple dose replications (Nelson and Holson 1978). Four inbred strains (C3H/He, C57Bl/6, Balb/C, and A/J) and one random-bred strain (CD-1) were treated daily by gavage with 15 to 120 mg/kg of technical 2,4,5-T on days 6-14 of pregnancy. Teratogenic effects were observed at 15 mg/kg in A/J mice and at 30 mg/kg in the other strains. For each strain, this was the lowest dose tested. There were significant differences in sensitivities between strains, and great variation between replications in the same strain with regard to induction of cleft palate, embyronic death, and fetal weight reduction. According to the authors, this variability may explain why studies on 2,4,5-T using small numbers of animals fail to demonstrate teratogenicity at low doses, although the same low dose levels of 2,4,5-T were shown to be teratogenic in this study.

In another recently completed study, Dow Chemical Company reported on the effects of 3, 10 or 30 mg/kg of purified 2,4,5-T (containing less than 0.5 ppb TCDD) on reproduction in Sprague-Dawley rats.*/ Exposure for three generations to 10 and/or 30 mg 2,4,5-T/kg per day resulted in statistically significant increases in the frequency of stillborn rat pups, and/or decreased survival of the pups that were born alive. No significant effects were observed at 3 mg/kg.

In summary, TCDD produces fetotoxic effects in test animals at the lowest doses tested. For example, maternal doses as low as 0.001 ug/kg in rats and 50 ppt in monkeys have increased lethality to fetuses. To date a no-observed effect level has not been found for TCDD-related effects on reproduction in any species tested. Exposure to purified 2,4,5-T with no detectable TCDD contamination (detection limit = 0.5 ppb) resulted in increased fetotoxicity at 10 mg/kg, with no significant effects in the same study at 3 mg/kg.*/

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*/ Dow has also claimed that the results of this study are confidential. See previous footnote on this subject.

Generally, a no-effect level is viewed as a toxicological endpoint, marking a level of exposure in animals which is "safe" because there are no observable adverse effects. Toxicologists generally assume that the animal no-effect level can serve as a base for estimating exposure levels which would be "safe" for humans. The "safe" level for humans is set at some level lower than the animal no-effect level to provide a "margin of safety" that takes into account differences in sensitivities between animals and humans, and differences in sensitivities among humans. This "margin of safety" does not represent an infallible indicator of potential hazard to humans. Error could be introduced because humans are more sensitive than the test species by a greater factor than normally allowed, or by the incorrect choice of a no-effect level.

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*/ The no-effect levels determined with purportedly "pure" 2,4,5-T have little value for assessing potential human risk from exposure to 2,4,5-T, since commercial 2,4,5-T contains TCDD. Therefore, it is prudent to assume that there is no no-effect level both for TCDD and 2,4,5-T containing TCDD.

The lowest level at which TCDD has no observable effects in test animals is crucial to the Agency's determination of the risk potential of 2,4,5-T. TCDD is present in this pesticide as a low-level contaminant and thus will be present in the environment at low levels whenever and wherever 2,4,5-T is used. If there truly were a no-effect level in animals, it would be reasonable to at least begin to estimate a possible "safe" level for humans and to assess the possible risk to humans by relating this assumed "safe" level to the level of the pesticide that may be in the environment, if that level is known. However, if there were no no-effect level, any use of 2,4,5-T would result in potentially significant exposure to TCDD, because there would be no minimum level upon which to estimate a margin of safety. Thus, because adverse reproductive effects have been reported at the lowest doses tested and because these doses approach the levels at which some humans may be exposed, any exposure to TCDD or 2,4,5-T containing TCDD must be considered potentially dangerous to the human fetus.

(2) Oncogenic Effects

As summarized in Section II, at the time of the 2,4,5-T RPAR, the Agency's Carcinogen Assessment Group (CAG) had available for assessment preliminary reports of two studies and one complete study. Dow Chemical Company studied the effects of TCDD on male and female

Sprague-Drawley rats exposed to 0.022, 0.21 or 2.2 ppb TCDD, and preliminarily reported that there were statistically significant increases in the incidence of hepatocellular carcinoma in female rats exposed to 2.2 ppb TCDD. In another study using Sprague-Dawley rats, Van Miller reported that 1 ppb and 5 ppb TCDD produced a carcinogenic response in the livers of male rats.*/

Since the 2,4,5-T RPAR was issued, CAG has had an opportunity to review the complete Dow study (Kociba et al. 1978) and has concluded that the combined incidence of hepatocellular hyperplastic nodules and hepatocellular carcinoma in rats is statistically significant at both the 2,200 and 210 ppt levels.**/ Also a more recent communication to CAG from the National Cancer Institute indicated that, in their as yet incomplete study, TCDD appears to be as carcinogenic and potent as was observed in the Dow study. In addition, CAG and others have compared the carcinogenic potency of TCDD with other known carcinogens. Based on these calculations, TCDD appears to be the most potent chemical carcinogen known (several times more potent than aflatoxin).

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*/ CAG (Memo 1979b) and an EPA audit found that this study had major shortcomings in design and conduct that limited the reliability of the data developed at dose levels lower than 1 ppb.

**/ Dow has also claimed that the raw data and/or results of this study are confidential. See previous footnote on this subject.

The Agency has examined the data showing that TCDD is carcinogenic at very low exposure levels in light of other information indicating that the use and distribution of 2,4,5-T to the environment creates opportunities for human exposure to these chemicals. In view of the non-threshold concept upon which the Agency cancer policy is based (Albert et al. 1977), any exposure to TCDD poses a significant risk of oncogenic effects occurring in the exposed population.

(3) Conclusion

In summary, available information supports the conclusion that there is a real potential for human risks due to exposure to 2,4,5-T and/or TCDD. These risks primarily relate to the oncogenic and fetotoxic effects of TCDD. Because TCDD is invariably present as a contaminant of commercial 2,4,5-T, any exposure to 2,4,5-T represents a significant potential risk to the exposed human population.

B. Exposure Resulting from the Use of 2,4,5-T

The use of 2,4,5-T results in the distribution of the pesticide to air, water, non-target vegetation, soil, and other environmental components in areas where people live and work. As a result, people and their food and water supplies may be exposed directly or indirectly to 2,4,5-T and its dioxin contaminant, TCDD. This section of the Position Document details information on the exposure potential resulting from the non-suspended uses of 2,4,5-T, particularly use on rice and rangeland. In some cases, information on exposure potential from these uses is derived from data on use practices, and in other cases this information is based on chemical residue data.

(1) Exposure due to 2,4,5-T Use on Rice

About 300,000 acres (12%) of the annual rice crop are treated with 2,4,5-T to control broadleaf and aquatic weeds. The major use areas are in Mississippi and Arkansas (93%), but some use occurs in Louisiana (6%), Missouri (1%), and California (<1%).

Greater than 99% of all application of 2,4,5-T for rice production is by fixed-wing aircraft which fly at speeds of 85 to 120 mph, 3 to 10 feet above the rice crop, when winds do not exceed 5 mph.

(a) Direct Exposure from Aerial Drift

The total rural population of the Delta region rice-growing counties is about 653,000 people with an estimated 222,000 people residing within 1/2 mile of rice fields, and an average rural population density of 40 people/square mile. When the use of the pesticide results in drift to areas of human work and habitation, people in these areas may be directly exposed to the pesticide by the inhalation and/or dermal routes.

Cotton farmers who live in the Delta rice-growing region have reported drift onto their cropland and related crop damage (30000/26:#302; #1888). These reports indicate that the pesticide has drifted beyond the spray area of the rice fields and into non-target areas. Such reports are consistent with studies showing that aerial application of other pesticides may result in drift for distances as great as 55 miles from the site of the spray operation (Akesson and Yates Undated).

(b) Contamination of Surface Waters

Application of 2,4,5-T to rice fields may result in contamination of rivers and streams. Rice fields are flooded with well water 2 to 4 inches deep and maintained at this level until about two weeks before harvest, except when producers drain their fields for an application of fertilizer in the middle of the growing season. About two weeks before harvest, the water is diverted from the fields to ditches from which the water eventually enters streams and rivers. 2,4,5-T contamination of these waters is demonstrated by data retrieved from the STORET system which indicate that 2,4,5-T residues are present in surface waters throughout the Delta region. Also, residues of 2,4,5-T have been detected in Louisiana by the National Surface Water Monitoring Program for Pesticides in the Tensas River at Tendal (12.9 ppb), the Red River at Alexandria (0.03 ppb), and the Calcasieu River near Lake Charles (0.03 ppb) during

August 1978. It is noted, however, that the monitoring programs do not distinguish between 2,4,5-T residues originating from rice, pasture, and rights-of-way uses in these areas.

In the Delta Region, especially in Louisiana, surface waters are a source of commercial and sport fishing. Although well water is recommended for crayfish confinement operations, surface water is sometimes impounded to flood the rice fields for the crayfish crop after the rice has been harvested. As a result, some the the 7.6 million pounds of fish and 24 million pounds of crayfish harvested annually in Louisiana may be cultivated in water contaminated with 2,4,5-T. This practice creates an opportunity for exposure to the local population which consumes more than 80% of the crayfish harvested each year in Louisiana. Estimates indicate that the average person in the Delta Region consumes 2.8 kilograms of freshwater catfish, mostly from local sources, each year.

Because surface waters in this area are used for drinking water and local fish cultivation, the Agency has considered these waters as a possible source of human exposure to 2,4,5-T. For example, in Louisiana rice-growing areas where 2,4,5-T is used, 6,000 people (<1%) derive their drinking water from surface sources. However, in rice-growing areas of Mississippi and Arkansas, the majority of the population obtains drinking water from deep wells.

The exposure of these populations would be greater if the ground water also is contaminated. However, because 2,4,5-T has a half-life ranging from 2 to 7 weeks, and TCDD residues though stable, are relatively immobile in soil, the Agency assumes that contamination of ground water from the rice use is generally unlikely.

(2) Exposure due to 2,4,5-T Use on Rangeland

(a) Use Practices and Populations Exposed

2,4,5-T is used on rangeland throughout the country, but major usage occurs in Arizona, Arkansas, Kansas, Missouri, New Mexico, Oklahoma, and Texas where about 1.4 million acres of rangeland are treated annually with 2,4,5-T. Estimates indicate that 47,000 people reside within 1/4 mile of the treated areas. Rural population density is generally 3 to 4 people/sq mi with one exception of 16 people/sq mi in central Missouri.

Ninety percent of the 2,4,5-T is applied by fixed-wing aircraft which fly at speeds of 85 to 105 mph, 10 ft above vegetation in winds that do not exceed 10 mph. The average spray droplet size is 300 microns, and drift control agents are used to reduce spray drift in 50% of the applications. Ground rigs and backpack spray units are used to treat small areas or especially troublesome areas. Droplet size ranges from 200 to 300 microns when applied with these units. Estimates indicate that about 0.1 to 6% of the spray would be 100 microns or less and could drift away from the target area when these methods are used to apply 2,4,5-T.

The amount and formulation of 2,4,5-T used depends on the kind of vegetation being treated and the density of the growth in the area (see Table 1). Both amine and low volatile ester formulations of 2,4,5-T and silvex are used, frequently in emulsions of water or oil during the spring and summer.

Rates of 0.5 to 2.0 pounds a.i./acre, in 1 to 4 gal/acre volumes are used, but 2 gal/acre volumes are used by 50% of the applicators. Average droplet size is 300 microns, and half of the applications are made with drift control agents. Treatment schedules vary from 1 to 3 consecutive years, depending on the severity of the problem, followed by retreatment 5 or more years later depending on the need.

(b) Water and Soil Residues

The STORET system contains data which show 2,4,5-T residues in water and sediment in the major rangeland use areas, and residues of 2,4,5-T have been reported in several Western streams during monthly monitoring for chemical residues at U.S. Geological Survey stations. However, because 2,4,5-T may have been used on rights-of-ways or pastures in the localities where the residues were detected, it has not been determined whether rangeland use of 2,4,5-T is the source of these residues. The National Surface Water Monitoring Program for Pesticides has not detected 2,4,5-T in surface water in these areas.

Studies indicate that 2,4,5-T residues on rangeland decline after application. For example, residues of 2,4,5-T on grasses immediately after application of 4 pounds/gallon, 3 gallons/acre at four sites in California, Michigan, North Carolina, and Texas ranged initially from 684 ppm to 1,668 ppm but declined to an average of 3 ppm after 16 weeks (Leng 1972). Residues of 2,4,5-T applied at 2 and 4 pounds a.i./acre in run-off water from cleared watersheds averaged 2.1 ppm three weeks after application but were below the limit of detection after two months (Lawson 1976). The hydrolytic half-life for 2,4,5-T has been estimated to be less than 14 days and about 2 to 7 weeks in soil. The half-life of TCDD residues is estimated to be one year in soil, but TCDD residues are not found deeper than 6 inches below the soil surface (Kearney et al. 1972; Helling et al. 1973).

(3) Exposure due to 2,4,5-T Use on Non-crop Sites

2,4,5-T is used to treat many broadleaf, herbaceous, and that may be present in a variety of urban and rural non-crop areas such as hedgerows, storage areas, and vacant lots. Recent data regarding the extent of 2,4,5-T used for these purposes is unavailable.

2,4,5-T is used throughout the country for this kind of weed control. The most common formulations are the low volatile esters. Ground rigs are used to treat large areas but hand held application devices are frequently used for spot treatments in small areas. The Agency has no estimate of the number of people that use 2,4,5-T or the number of people in the immediate vicinity of these spray sites because of their heterogeneous nature.

Exposure for this kind of usage appears to be confined to the applicator and those people residing or working in the immediate vicinity of the spray area. Information from studies of forest workers who apply phenoxy-herbicides with backpack sprayers indicates that it may be possible for the applicator to contact 0.8 ppb of the chemical spray due to dermal exposre and 0.3 ppb due to inhalation exposure (Lavy 1978). Therefore, the Agency is concerned about the exposure that may result due to direct contact as well as drift.

Table 1. 2,4,5-T Application Rates on Rangeland by Different Treatment Methods

Application Site	Application Method	Region Applied	Application Rate	Number of Applications
Mesquite	Aerial	South Texas Plains	0.67 pounds acid equivalent per acre	3 consecutive seasons; retreatment in 16 years
		Rolling Plains of Texas and Oklahoma	0.5 pounds a.e./acre	one application; retreatment in 8 years
		Rolling Plains of Texas and New Mexico	0.5 pounds a.e./acre	one application; retreatment in 10 years
		Gulf Coast and Coastal Prairie	1 pound a.e./acre	one application; retreatment in 5 years
		South Texas Plains	1 pound a.e./acre	one application; retreatment in 5 years
			1 pound a.e./acre of 2,4,5-T + picloram (50:50)	one application; retreatment in 5 years
		Southwest	0.5 pounds a.e./acre	one application; retreatment in 10 years
Post and Blackjack Oak Savannah	Aerial		2 pounds a.e./acre	one application; retreatment in 5 years
			2 pounds a.e/acre 1st year & 1.5 to 2 pounds a.e. per acre 2nd year	one application; retreatment in 10 years

Table 1. Continued

¶Application ¶Site	Application Method	Region Applied	Application Rate	Number of Applications
¶Hardwoods ¶within ¶Post and ¶Blackjack ¶Oak ¶Savannahs	Aerial		2 pounds a.e./acre	for 2 seasons; retreatment in 10 years
¶Sand Shinnery ¶Oak			0.5 pounds a.e./acre	for 2 seasons; retreatment in 10 years
			0.5 pounds a.e./acre	one application; retreatment in 5 years
¶Cactus			2 pounds a.e./acre	retreatment in 20 years
¶Yucca			0.67 pounds a.e./acre	retreatment in 10 to 15 years
¶Mesquite ¶and Oak	Broadcast Ground Application		2 pounds a.e./acre	one application; retreatment frequency varies from 5 to 10 years
¶Yucca			0.67 pounds a.e./acre	one application; retreatment in 10 to 15 years
¶Mesquite, ¶Oaks, and ¶other ¶species	Spot Treatment		8 to 16 pounds aehg oil for bark treatment, or 6 to 8 pounds aehg water-oil emulsions for basal-stem treatments	

C. Epidemiologic Data

The risk assessment for 2,4,5-T is based in part on data showing that exposure to 2,4,5-T and/or TCDD results in tumors, and dead and deformed offspring in test animals, and that the uses of the pesticide create opportunities for exposure to humans. Together these facts suggest that if the use of the pesticide results in human exposure, humans who live and work in areas of use may experience the kinds of adverse health effects observed in test animals.

This reasoning is borne out by the results of a recent epidemiological study which reported that women living in the vicinity of Alsea, Oregon, have a statistically significant higher incidence of spontaneous abortions (miscarriages) than women living in a control area. Alsea is an area in which two dioxin-containing pesticides, 2,4,5-T and silvex are used extensively for forest management and on rights-of-way. Additional analyses of the data indicate that there is a significant correlation between the use of 2,4,5-T in the study area and the subsequent increase in the rate of spontaneous abortions in the study area.*/

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*/ The Alsea study was analyzed using 2,4,5-T data. However, the serious implications of this study are as applicable to silvex as to 2,4,5-T, because TCDD, the contaminant contained in both herbicides, is a potent mammalian fetotoxin and teratogen at very low doses. Conversely, silvex and 2,4,5-T are fetotoxic and teratogenic at comparatively higher doses. It is reasonable to assume that the adverse human reproductive effects observed in Alsea, which have been attributed to low-level exposure to 2,4,5-T, are due primarily, or at least in part, to the TCDD in the 2,4,5-T. Therefore, since silvex also contains TCDD, it is prudent to conclude that the Alsea data are applicable to silvex use when evaluating potential reproductive risk to humans. [See 44 FR 15904].

This relationship between exposure to 2,4,5-T spraying and an increased incidence of miscarriages in humans is not surprising. This is the same relationship that has been demonstrated to exist in test animals through numerous animal studies. While there are uncertainties concerning the amount of 2,4,5-T and/or TCDD to which the Alsea area women may have been exposed and concerning the precise route (or routes) of human exposure, the statistically significant incidence of miscarriages described above, coupled with the uncontestable data from the animal studies, makes it reasonable to conclude that women in the Alsea study area may be exposed to, and adversely affected by, 2,4,5-T, silvex and/or TCDD. Moreover, it is also reasonable to assume that the same type of effects may occur wherever and whenever 2,4,5-T or silvex containing TCDD is used.

Further, the Alsea experience may not be an isolated incident. Reports of people adversely affected by exposure to phenoxy herbicides and/or TCDD have frequently appeared in medical and scientific journals. Recent summaries appear in IARC, NRCC, and U.S. Air Force documents on phenoxy herbicides and dioxins. In addition, as a result of the 2,4,5-T RPAR, the Agency has received numerous accounts of adverse human health effects which the reporters attributed to phenoxy herbicides and/or TCDD. The cumulative effect of these reported incidents suggests that people who live and/or work in areas of 2,4,5-T use may experience adverse health effects.

IV. Preliminary Benefits Analysis of 2,4,5-T Use on Rangeland, Rice, and Non-crop Areas

A. Introduction

This preliminary analysis is an economic assessment of the impact of the cancellation of 2,4,5-T for use on rangeland, rice, and non-crop uses. The analysis assumes that silvex also will be cancelled for these uses. In view of the virtually identical toxicological characteristics of the two compounds and the similar nature of the benefits for both, it is unlikely that one would be cancelled and not the other.

The information relating to the benefits of 2,4,5-T used in this report was derived principally from a single source: The Biologic and Economic Assessment of 2,4,5-T ("USDA Assessment Report") [USDA 1979].[*]

In addition, benefits information submitted by registrants, users, and other parties in response to the RPAR notice on 2,4,5-T was used in the analysis where appropriate.

There are some disadvantages to the heavy reliance of this analysis upon the USDA Assessment Report for the rangeland and rice information. As is commonly the case in assessing benefits of pesticides, the available information reported and analyzed in the USDA Assessment Report was a mixture of empirical data and expert opinion and did not lend itself to precise statistical analysis. Thus, the estimates reported in this analysis and based on the USDA Assessment Report represent rough predictions of the impact of cancellation. The lack of confidence intervals or error terms does not imply exact precision. The estimates are merely approximations of the projected impacts, within the limitations of the data and analyses.*/

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[*] This report was prepared jointly by the USDA-States-EPA 2,4,5-T Assessment Team, established pursuant to a memorandum of understanding between USDA and EPA.

The general approach of this analysis is to evaluate the impacts of shifting to alternatives at the user level and projecting these impacts to the market and consumer levels where appropriate. Impacts on users are considered on a per-unit, per-establishment basis, and at state, regional, and national levels.

B. Summary of Findings

(1) Rangeland

There are an estimated one billion acres of rangeland

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*/ The Agency is continuing to collect and review data relating to the benefits of 2,4,5-T for rice, range and non-crop uses.

and pasture[*] suitable for grazing in the contiguous 48 states, plus 351 million acres in Alaska and 3 million acres in Hawaii. About 90 percent of this total acreage is rangeland. Of this total, about one percent is treated with herbicides, primarily 2,4-D.

2,4,5-T is used to control various woody and herbaceous plants on about 1,500,000 acres of rangeland. The most important weed species treated are mesquite and several species of oak. Cactus, yucca, poisonous plants, and desert shrubs are also treated with 2,4,5-T to a lesser extent.

The estimated impact on farm income and beef prices of cancelling 2,4,5-T on range would be slight. When compared with the U.S. total farm value of beef production (about $15 billion annually), these impacts, averaging less than $16.5 million annually, are relatively small (0.1 percent). In those local areas where target weed species are a problem, local farm income may be affected significantly. Adequate information to evaluate such local impacts is not available. At the retail level, cancellation of 2,4,5-T for use on rangeland could cause the consumer price index for food and beverages to increase by a maximum of 0.05 percent, an insignificant increment.

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[*] "Rangeland" is land producing forage for animal consumption harvested by grazing, which is not cultivated, seeded, fertilized, irrigated, or treared with pesticides or other such similar practices on an annual basis. Fencerows enclosing range areas are included as part of the range. This precludes land listed in the definition of pasture. "Pasture" is land producing forage for animal consumption, harvested by grazing, which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application and other similar practices applied to it. Fencerows enclosing the pastures are included as part of the pasture.

(2) Rice

Over 99 percent of the 2.5 million acres of U.S. rice-growing acres are located in Arkansas, Louisiana, Texas, Mississippi and California. 2,4,5-T is currently used to control broadleaf and aquatic weeds on an estimated 300,000 acres in the lower Mississippi Valley area comprising about 12 percent of U.S. rice acres.

Propanil and 2,4-D are the most likely substitutes for 2,4,5-T for control of rice weeds. These chemicals are thought to be generally less effective than 2,4,5-T for control of the major rice weeds; thus yield and quality reductions may occur where propanil and 2,4-D are used to replace 2,4,5-T. The substitution of these chemicals for 2,4,5-T could result in production reductions of less than 0.1% of national production.

If 2,4,5-T is cancelled for use on rice, annual producer weed control cost increases and production losses are estimated at about $6 million per year.
Prices received by farmers, and ultimately paid by consumers, could increase by about five percent within three years. Since rice comprises only a small portion of the U.S. consumer's diet (consumption of milled rice is less than eight pounds per capita annually), price increases of this magnitude will have only minor impacts on consumers.

(3) Non-crop Uses[*/]

2,4,5-T is registered for control of many broadleaf and herbaceous weeds in a variety of urban and rural non-crop areas such as hedgerows, storage areas, and vacant lots. It is believed that only about 11% (190,000 acres) of all non-crop areas treated with herbicides are treated with 2,4,5-T annually.

Both chemical and non-chemical controls are available as alternatives to 2,4,5-T for chemical control in non-crop areas. The chemical alternatives include 2,4-D, picloram, dicamba, AMS, and amitrole. Non-chemical controls include mechanical methods, such as mowing or shearing, and manual methods. The relative efficacy of the alternatives in comparison to 2,4,5-T is unknown. However, it is believed that chemical alternatives, either in multiple applications or in combination, will be widely substituted for 2,4,5-T and will provide equivalent control.

[*/] "Non-crop uses" include: airports; fences, hedgerows not otherwise included among the previously suspended uses, e.g., rights-of-way, pasture); lumber yards; refineries; non-food crop areas; storage areas; wastelands (not otherwise included among the previously suspended uses, e.g., forestry); vacant lots; tank farms; industrial sites and areas (not otherwise included among the previously suspended uses, e.g., rights-of-way).

C. General Production and Use Patterns

(1) Production, Imports, and Exports

2,4,5-T is produced domestically by The Dow Chemical Company, Rhodia, Inc., Thompson-Hayward Chemical Co., and Transvaal Inc. Since 1970, 2,4,5-T production has declined. Current production is in the range of 7.0 to 9.0 million pounds annually. Imports of 2,4,5-T in 1977 were estimated at 670,000 pounds, well above the 341,000 pound average for the previous five years. Total domestic use of 2,4,5-T is estimated to have been about 9.0 million pounds of active ingredient for 1977.

(2) Quantitative Usage Analysis

The use of 2,4,5-T on rangeland and rice comprises about 23 percent (2.1 million pounds) of the estimated 9.0 million pounds of 2,4,5-T active ingredient used annually and 38 percent (1.8 million acres) of the 4.7 million acres treated annually with 2,4,5-T (Table IV-1). Rangeland use of 2,4,5-T accounts for 20 percent of the active ingredient and 31.9 percent of the acres treated; however, only 0.2 percent of grazing acreage in the U.S. is treated annually with 2,4,5-T. Rice usage of 2,4,5-T (300,000 pounds on 300,000 acres), while minor compared with the extent of usage on rangeland, represents nearly 12 percent of the U.S.

rice acreage and about 28 percent of rice acres in the lower Mississippi Valley area. Recent data on the use of 2,4,5-T for non-crop areas is not available. However, a 1974 report indicates that 2,4,5-T and 2,4,5-T + 2,4-D products combined were used on a total of 190,000 acres, or only 11% of the total 1.8 million acres treated with one or more of 15 chemicals for grounds maintenance on these sites.

Table IV-1. Quantitative Usage Analysis of 2,4,5-T

		Extent of Use*				
Site	Estimated U.S. Acreage (millions acres)	Active Ingredient (pounds) (million)	Active Ingredient (Pct)	Units Treated (acres) (million)	Units Treated (Pct)	Acres Treated As a Percent of Total U.S. Acres
Range	900.0	1.8**	20.0	1.5	31.9	0.2
Rice	2.5	0.3	3.3	0.3	6.4	12.0
All Sites***	—	9.0	100.0	4.7	100.0	—

* USDA-1979.

** Includes both aerially and ground applied. Approximately 1.6 million pounds are aerially applied.

*** Includes estimated usage on Rights-of-way, Pasture, and Forestry.

D. Preliminary Benefit Analysis of 2,4,5-T Use on Rangeland

(1) Current Use

A wide variety of herbaceous and woody plants grow on rangelands. The major weed species controlled with 2,4,5-T, such as mesquite, post oak, blackjack oak, and sand-shinnery oak, compete with the desired forage species for nutrients, water, space and light. Other important species controlled with 2,4,5-T are cactus, miscellaneous hardwoods and plants poisonous to livestock. The most serious problems, and the majority of 2,4,5-T use, occur on rangeland in the southwestern U.S.

Estimates of acres treated are available only for the major weed pests treated with 2,4,5-T; thus, the analysis is limited to the use of 2,4,5-T to control mesquite and various oak species. Of about 93 million acres of mesquite-infested rangeland in the Southwest, an estimated 570,000 acres are treated with 2,4,5-T annually. This figure includes about 183,000 acres treated with mixtures of 2,4,5-T and picloram. Over the life of the control cycle for mesquite, about 5.4 million acres are treated with 2,4,5-T.

The post-blackjack oak savannah infests about 35 million acres in Texas, Arkansas, Oklahoma, Kansas, and Missouri. An estimated 460,000 acres of this savannah area are treated with 2,4,5-T (920,000 pounds) annually for control of post and blackjack oaks. Over the life of the control cycle, an estimated 2.3 million acres are treated.

Sand-shinnery oak infests about 14 million acres in Texas, Oklahoma, and New Mexico. Each year, about 382,000 acres are treated with 2,4,5-T (382,000 pounds). Over the life of the control cycle, 3.8 million acres are treated.

2,4,5-T is applied both aerially and by ground methods on range. This analysis evaluated only aerial application for the control of mesquite and the specified oak species on rangeland in the southwestern U.S. Aerial applications are believed to account for the vast majority of 2,4,5-T treated acres. For mesquite control by aerial application, dicamba is likely to be the most viable alternative to 2,4,5-T. There is no registered and effective substitute for aerial treatment of the oak species.

Other registered chemical alternatives as well as non-chemical controls not analyzed here are effective against one or more of the various range weeds controlled by 2,4,5-T. However, these chemicals are either not registered for aerial use or are not effective when applied aerially. Thus, these alternatives are not likely to replace the majority of 2,4,5-T use. Where ground application, especially spot treatment, is adequate, one or more of these alternatives will generally provide effective control depending on the nature and complexity of the weed problem. Thus, the alternatives, other than dicamba, may provide some weed control in the absence of 2,4,5-T for rangeland.

The following analysis is based on an assumption that dicamba will be the primary alternative to 2,4,5-T. The use of this assumption reflects the utility of dicamba for aerial treatments, the prevalent method of application of 2,4,5-T. Economic impacts of the cancellation of 2,4,5-T on rangeland using ground application methods has not been quantitatively evaluated. However, since very few acres are treated by this method and because alternatives are available, the impact of cancellation would be quite small.

To control mesquite, 2,4,5-T aerial application rates vary from 0.5 to 1.0 pounds acid equivalent (a.e.) per acre applied alone and 0.25 to 0.5 pounds a.e./acre applied in combination with picloram. To control oak, aerial application rates vary from 0.5 to 2.0 pounds a.e. per acre for 2,4,5-T. An estimated 1.6 million pounds a.e. of 2,4,5-T are applied to control these weeds annually--340,300 pounds to control mesquite and 1.3 million pounds to control oaks.

The quantity of dicamba used currently on rangeland is not known. However, the USDA Assessment Team predicted that if 2,4,5-T were cancelled, an estimated 217,000 pounds a.e. of dicamba would be used annually to control mesquite.

(2) Evaluation of 2,4,5-T and Alternatives

Information, including research, from experts on the USDA Assessment team suggests that dicamba is as effective as 2,4,5-T against mesquite in some areas. In other areas, the experts believed dicamba would not be effective. No other registered chemical is believed to be effective against oaks when applied aerially. Substitute treatment of oak infested acres would be limited to more expensive ground application treatments. It is likely that on many acres treatments will be foregone.

In those areas where dicamba would be as effective as 2,4,5-T against mesquite, no yield effects would occur. Beef production would be reduced on those acres where dicamba was not effective against mesquite and on oak infested acres not treated. Thus, it was estimated that total U.S. production losses would be about 21.5 million pounds of beef in the first year and would increase progressively during each of the following years until other alternatives become available.

Equally concentrated solutions (4 pounds a.e./gal.) of 2,4,5-T and dicamba cost $15 and $36 per gallon, respectively. This difference in herbicide material cost is reflected in increases in the total application cost for mesquite control. For example, at an application rate of 0.5 pounds a.e. per acre, the aerial application cost, including herbicide material, diesel oil, flaggers, and application is $4.35 per acre for 2,4,5-T and $6.85 per acre for dicamba.

Table IV-2. Costs of Aerially Spraying 2,4,5-T and Dicamba

¶	Farm	Application	Application Cost		¶
¶Herbicide	Price	Rate	Herbicidal Material	Total[a]	¶
¶	$/gal.	lbs./acre	- - - - - - - -$/acre- - - - - -		¶
¶					¶
¶2,4,5-T	15	0.50	1.88	4.35	¶
¶		0.67	2.51	4.75	¶
¶		1.00	3.75	6.75	¶
¶		2.00	7.50	11.00	¶
¶					¶
¶Dicamba	36	0.50	4.50	6.85	¶

[a] Includes herbicide, diesel oil, flaggers and applications.
Source: USDA-1979.

(3) Economic Impact

(a) User Impacts

The economic impacts at the user (ranch) level were estimated for six delineated mesquite areas and two oak areas. The areas were delineated on the basis of differences in woody plant species, beef production, stocking rates, life span of treatment, and various other factors. The effects of cancelling 2,4,5-T were estimated over a 16-year period and discounted to 1978.

The 16-year period was chosen as a convenient long-term period because in some areas 2,4,5-T treatment provides control for 16 years. One disadvantage of projecting impacts over a long period in which all factors are assumed to remain constant is the possibility, if not the likelihood, that new control techniques and/or tools (chemical or non-chemical) will come into use during that period. In addition to the chemical alternatives now registered for range use, several promising herbicides are currently under review for registration. Economic impacts could be substantially reduced by the advent of cheaper or more efficacious controls than the alternatives initially evaluated. It is not now possible to assess the impact of potential alternatives upon future range weed control practices.

The cancellation of 2,4,5-T for control of mesquite and oaks could result in increased control costs, decreased beef production or both. The estimated first-year impacts of 2,4,5-T cancellation is $5.6 million. The cumulative 16-year estimated impact, discounted at a 7 percent rate and expressed in 1978 dollars is $262.5 million. (Note items 2, 3, and 4 under "Limitations and Assumptions," below). If no control is practiced, the 16-year impact is estimated to be $347.5 million.

On a per-acre basis, the reduction in average annual returns from beef production in different areas are estimated to range from 3.6% to 42% if dicamba replaces 2,4,5-T. If no control is used, the change in value of beef production varies from a gain of $0.10 per acre in one area to a reduction of $6.53 per acre in another area.

(b) Market/Consumer Impacts

The market and consumer impacts of the cancellation of 2,4,5-T were evaluated using a standard, computerized beef marketing model to simulate the markets. The model used the liveweight livestock production impacts from the USDA Assessment Report and estimated market and consumer impacts after allowing normal adjustments in the marketplace. Based on historical data, market prices and consumption were predicted for 12 years into the future, assuming all factors remain constant. Impacts were then measured as changes caused by cancellation of 2,4,5-T and silvex.

During the early years following cancellation, beef slaughter (and domestic consumption) was estimated to rise as affected ranchers reduced their herd size. The temporary increase in supply was reflected in depressed beef prices. Then, after the fifth year, as the market continued to adjust, beef slaughter declined and prices rose.

Over the 12-year period, the change in prices for utility cows and choice steers at Omaha varied from a low of -0.03 percent to a high of 0.36 percent. The change in prices averaged $0.06/cwt ($0.0006/pound). The Wholesale Price Index for Farm Products was higher by an average of 0.084 percent annually.

Domestic disappearance of nonfed beef averaged 25 million pounds higher than the control condition for the first five years and 21 million pounds lower than the control condition during the next seven years. Over the 12-year period, there was an average annual reduction of 1.7 million pounds of nonfed beef. This reduction amounted to 0.025 percent of domestic disappearance of nonfed beef (6.8 billion pounds annually) and 0.007 percent of total domestic disappearance of beef (fed and nonfed; 25.2 billion pounds annually).

At the consumer level, the Consumer Index for Food and Beverages increased by no more than 0.046 percent in any year and had an average increase of 0.03 percent annually.

Based on the fractional changes in prices and consumption attributed to cancellation of rangeland uses of 2,4,5-T, the market and consumer level impacts would be insignificant.

(c) Limitations and Assumptions

In addition to the limiting factors discussed in the general introduction to this economic analysis, the following specific limitations and assumptions are applicable to the foregoing market/consumer impact analysis.

1. The economic assessment is taken from the USDA Assessment Report. Since the completion of this evaluation, there has been some reinterpretation of the base acreages treated with 2,4,5-T. Some of the mesquite acreage reportedly treated with 2,4,5-T (single active ingredient) was actually treated with a combination of picloram and 2,4,5-T. Similarly, for the oaks, some acreage reportedly treated with 2,4,5-T

was treated with silvex. This assessment includes the most recent estimates of acreage treated with 2,4,5-T, picloram + 2,4,5-T, and silvex. The total acreage evaluated, either for individual areas or in the aggregate, has not changed.

However, the picloram + 2,4,5-T combination is more expensive than 2,4,5-T alone. Therefore, the effect of this change is to increase the base cost-of-control (current situation) and reduce the estimated economic impact. The exact amount of this reduction has not been calculated, but the acreage involved and the cost difference per acre do not appear large enough to affect the basic conclusions of this report. If 2,4,5-T is cancelled, dicamba will be the major alternative in those areas and on those weed species where it is effective.

2. The analysis was limited to weed species evaluated (mesquite and selected oaks), the method of application (aerial), and the geographic area (southwestern U.S.). However, it is believed that this analysis accounted for the majority of 2,4,5-T used on U.S. rangeland.

3. Benefits were estimated solely on the basis of beef production, although control of weeds with 2,4,5-T may also produce other benefits in terms of increased watershed yield and possible adverse effects on wildlife production. It was not possible to quantify these factors based on available information.

4. In discounting future net returns it was assumed that no new alternative controls would become available, no adjustments in management practices would substitute for 2,4,5-T, and no technological changes in beef production would occur during the 16-year period of analysis. In the short-term this assumption may be realistic but in the long-term, e.g., greater than 5 years, it is not. Other chemicals are currently being tested, and it is likely that one or more of these would be registered within a few years.

5. This analysis did not quantify localized impacts which are likely to result from a cancellation of 2,4,5-T.

6. Costs of production, other than weed control costs, were assumed to remain fixed regardless of changes in herd size. In reality, some of these costs, e.g., supplemental feed or pond maintenance, are variable, increasing or decreasing with changes in herd size.

E. Preliminary Benefit Analysis of 2,4,5-T Use on Rice

(1) Current Use

(a) Pest Infestation and Damage

Weeds reduce the yield and quality of rice in the U.S. by an estimated 15 percent each year on about 2.5 million acres; the average yearly loss was valued at about

$165 million during the 1975-1977 period. The cost of using herbicides to prevent greater losses was about $60 million each year during the same period. The cost of cultural practices (including crop rotation, land preparation, irrigation, and fertilization) during this period, was estimated at $70 million. Thus, the total estimated direct losses and expenditures for weed control were $295 million annually for the 1975-1977 period.

Conditions favorable for growing rice also favor the growth and reproduction of many terrestrial, aquatic, and semi-aquatic weeds. Weeds in rice produce an abundance of seed. Once these infest the land, they are difficult to remove and may remain viable in the soil for many years. Rice weeds reduce yields by direct competition and reduce quality through contamination of the harvested grain with weed seeds.

The principal weed pests for which 2,4,5-T use is most important include hemp sesbania, northern jointvetch, morningglory, ducksalad, and redstem. Without weed control it is estimated that 13% yield and 4% quality reductions on rice in the 2,4,5-T use area would occur.

(b) 2,4,5-T and Alternatives

Herbicides registered for use in rice may be classed into three groups: (1) those that control grass weeds (propanil and molinate); (2) those that control broadleaf and aquatic weeds (2,4,5-T, 2,4-D, MCPA, silvex, and bentazon); and (3) those that control a combination of grass, broadleaf, aquatic, and sedge weeds (bifenox and oxadiazon). The pesticides in the last group of herbicides were registered for use on rice only recently, and they are usually combined with propanil to achieve satisfactory control. Copper compounds (copper sulfate and copper complexes) are used for control of green and blue-green filamentous algae in rice, but the efficacy of these compounds is erratic. Endothall is registered and used only in California for the control of submerged aquatic weeds in rice; it is not effective on the immersed aquatic weed complex in the lower Mississippi Valley area.

Cultural practices and other non-chemical means may be practical for control of weeds in some circumstances and could mitigate some of the economic impacts that might result from the cancellation of 2,4,5-T. However, these alternatives have not yet been evaluated in depth. Thus, the following analysis is based on the assumption that only chemical alternatives would be used to replace 2,4,5-T.

(c) Use of 2,4,5-T and Chemical Alternatives

Based on information collected by experts on the USDA Assessment Team, it was estimated that about 98% of the 2.5

million U.S. rice acres receive one or more annual applications of herbicides for control of rice weeds. Currently, 2,4,5-T is applied to an estimated 300,000 acres annually. This amounts to only 12% of all rice acres treated with herbicides. At the most common application rate of one pound of 2,4,5-T a.e. per acre, 300,000 pounds of 2,4,5-T are used annually.

Virtually all 2,4,5-T use on rice occurs in four lower Mississippi Valley states (Arkansas, northern Louisiana, Mississippi, and Missouri). The majority of rice acre-treatments of 2,4,5-T were applied in Arkansas (177,000 acres) and Mississippi (101,000 acres) with a lesser number of acre-treatments in northern Louisiana (18,000 acres) and Missouri (4,000 acres). The rice acreage treated with 2,4,5-T in each state ranges from three percent in Louisiana to 71 percent in Mississippi, with 21 and 25 percent in Arkansas and Missouri, respectively. Major rice producing areas of Texas and California, where 37 percent of U.S. rice is produced, use little or no 2,4,5-T.

Expenditures for 2,4,5-T use on rice (1975-77 period) averaged approximately $3 million annually or about five percent of total U.S. rice herbicide expenditures. Expenditures for rice herbicides, including application costs, generally averaged $60.8 million annually during the 1975-77 period.

(2) Evaluation of 2,4,5-T and Alternatives

(a) Comparative Efficacy and Yield Effects

2,4,5-T is thought to provide somewhat better control of broadleaf, aquatic, and sedge weeds than other herbicides. It is also believed to be less injurious to non-target crops (cotton and soybeans) than the other phenoxy herbicides, 2,4-D, MCPA, and silvex.

2,4-D is thought to be comparable to 2,4,5-T in controlling most broadleaf, aquatic, and sedge weeds and would be used more frequently if it were not highly injurious to cotton. Most rice-growing states regulate the aerial application of 2,4-D to reduce the damage to nearby cotton fields caused by spray drift. Therefore, 2,4-D could be used on only about half of the rice acreage now treated with 2,4,5-T. 2,4-D does not control northern jointvetch as effectively as 2,4,5-T and is ineffective on grass weeds.

Yield and quality losses could average two and one percent above current losses respectively, if 2,4-D were substituted for 2,4,5-T for use on rice-growing acres during the first three-year cropping cycle. During the second three-year period, yield losses could average four percent annually, and quality losses could average two percent annually.

Several other herbicides used for control of rice weeds include molinate, MCPA, bifenox, bentazon, and oxadiazon. Molinate is not thought to effectively control hemp sesbania, northern jointvetch, ducksalad, morning glory or redstem. MCPA is not used in the Lower Mississippi Valley area since it is believed to be relatively ineffective on hemp sesbania, northern jointvetch, and Indian jointvetch. Bifenox, bentazon, and oxadiazon are three new herbicides which are currently used to a limited extent; they are not believed to be as effective as 2,4,5-T on most broadleaf and aquatic weeds.

Cultural/mechanical weed control practices include summer fallowing, seedbed preparation, crop rotation, special seeding methods, management of irrigation water, cultivation, and handweeding (in sparse weed infestations or in small isolated areas). Effective weed control systems in rice should combine preventive, cultural, mechanical, and biological methods with chemical control methods. Weed management systems which omit any one of these components are often inadequate and may fail to control weeds effectively.

While some cultural/mechanical practices are effective on some rice weeds without the use of chemicals, most are not dependable or predictable tools as sole alternatives to the use of chemical herbicides.

(b) Comparative Costs

Estimated costs for using 2,4,5-T and alternative herbicides in the lower Mississippi Valley areas during 1975-77 are summarized in Table IV-3. 2,4,5-T costs are estimated at $9.50 per acre compared with $7.40 per acre for 2,4-D and $12.90 to $21.80 per acre for propanil. Bentazon, molinate, and oxadiazon material and application costs range from $13.50 to $13.90 per acre, while bifenox costs are estimated at $21 per acre.

Table IV-3. Estimated Cost of Using 2,4,5-T and Alternate Herbicides in Rice Areas, Southern Rice Producing area, 1975-1977

Item	Unit	Herbicide								
		2,4,5-T	Propanil*		Molinate	2,4-D	Silvex	Bifenox	Bentazon	Oxadiazon
			1 appl.	2 appl.						
Quantity	pounds	1.0	3.0	6.0	3.0	1.0	1.0	3.0	0.75	0.75
Cost per pound	dollars	5.50	3.30	3.30	3.70	3.40	5.50	6.00	14.00	14.50
Herbicide cost per acre	dollars	5.50	9.90	19.80	11.10	3.40	5.50	18.00	10.50	10.90
Application cost per acre	dollars	4.00	3.00	3.00	2.75	4.00	4.00	3.00	3.00	3.00
Total Herbicide cost	dollars	9.50	12.90	21.80	13.85	7.40	9.50	21.00	13.50	13.90

* One application of 3 pounds/acre controls many broadleaf weeds; two applications at 3 pounds/acre each control weed grasses.

SOURCE: Data adapted from Table 22, Page 4-79, USDA 1979.

(3) Economic Impact

(a) User Impacts

The following assumptions and limitations, in addition to those noted in the general introduction, are specifically applicable to the following rice user impact analysis.

(1) The analysis was limited to aerial application of 2,4,5-T, which accounts for 97.3 percent (292,000 acres) of current use. Ground application, accounting for 2.7 percent or 8,000 acres of 2,4,5-T use, were not evaluated due to data limitations.

(2) To reduce the year-to-year variability of climatic and market effects, statistics for acres harvested, per-acre production, farm level prices, and herbicide material and application costs were based on 1975-77 averages. These averages were assumed to be representative of impacted acres.

(3) To demonstrate short and mid-term effects of weeds in rice if 2,4,5-T is cancelled, two cycles of rice-soybean rotations (one year rice and two years soybeans) were considered.

Yield and quality impacts were estimated by the USDA Assessment Team for the first and second three-year crop rotation periods (1978-83). Estimated revenue impacts were discounted to present value using a seven percent discount rate.

(4) Crop production budgets, based on the opinions of research and Agricultural Extension Service personnel in rice producing areas, were used to estimate cost differences between 2,4,5-T and alternative weed-control programs.

(5) This analysis assumes no new herbicides will be registered to control rice weeds during the six-year impact period.

If 2,4,5-T is cancelled for use on rice, producers would most likely shift to weed control programs utilizing 2,4-D and propanil. Yield and quality reductions might result on those acres treated with 2,4-D and propanil because these herbicides are thought to be less effective than 2,4,5-T.

Weed-control cost increases and production losses without 2,4,5-T are estimated at $5.0., $4.7, $4.4, $6.8, $6.3 and $5.9 million, respectively, during the first six years following cancellation. The total value of rice in the lower Mississippi Valley averaged more than $0.5 billion per year between 1975-77. Thus, in this four-state area economic impacts would range from 0.8 to 1.2 percent of the value of production. The estimated impact on U.S. rice production if 2,4,5-T is cancelled is minor, ranging from 0.04 to 0.08 percent.

During the first three-year period, estimated annual increased costs and production losses range from $12 to $21 per acre in the lower Mississippi Valley area for a weighted average of $14 per acre. During the second three-year period, estimated annual per-acre impacts range from $20 to $31 for a weighted average of $23 per acre.

Based on information from the USDA Assessment Team Report, an average of 46 acres of rice per farm in the lower Mississippi Valley area are treated with 2,4,5-T. During the first three-year period, annual losses on these 46 acres could total about $644 or 15.2 percent of net revenue per rice acre. During the second three-year period, the average annual loss on these 46 acres of rice could total $920 or 21.7 percent of net revenues per acre.

(b) Consumer and Market Impacts

The Data Resources Inc. (DRI) Model of U.S. agriculture was used to estimate regional and national producer impacts, in terms of changed cash prices and domestic disappearance of rice if 2,4,5-T and silvex are cancelled for use on rice.

The DRI model dynamically solves for national acreage, yield, production, domestic use, export use, ending stocks, cash prices and farm prices of rice. The model is not region-specific in rice production variables. However, it is possible to solve the national model by making adjustments in the appropriate yield and acreage factors in the model and solving the model under these new conditions.

For purposes of this analysis, the following methodology and assumptions were used to make factor adjustments in the DRI model.

(1) Rice production and control cost changes as estimated by the USDA Assessment Report were used to adjust initial values in the DRI model.

(2) Based on net revenue data from the USDA Assessment Report, users of 2,4,5-T in rice-producing areas of Louisiana, Mississippi, and Missouri could shift from rice to soybean production as competition from 2,4,5-T controlled weeds increased. For the Consumer and Market analysis, rice producers in this area were assumed, at the

outset, to shift from rice to soybean production. Rice producers in Arkansas were assumed to continue rice production since rice, treated with alternatives to 2,4,5-T, is more profitable than soybeans.

(3) The DRI model was solved dynamically from the fourth quarter of 1978 through the fourth quarter of 1990 assuming 2,4,5-T and silvex are cancelled and all other alternatives are available.

Louisiana, Mississippi, and Missouri rice producers who shift from rice to soybean production could have revenue reductions ranging from $18 to $29 per acre on 120,000 acres. The addition of 120,000 acres to U.S. soybean production is small relative to total national soybean acreage (60 to 70 million acres); thus measurable impacts on soybean production or prices are unlikely.

Arkansas rice producers using 2,4,5-T will continue to produce rice rather than soybeans since rice is more profitable under any alternative weed control strategy. If 2,4,5-T is cancelled, the value of production net of treatment costs will decline by about 4.2 percent in 1980 ($2.3 million) and 2.2 percent in 1981 ($1.3 million). By 1982, the estimated value of rice production, net of treatment costs, approaches the pre-cancellation levels. Projected prices received by both 2,4,5-T users and non-users, responding to lower rice production, increase 1.4., 3.2 and 4.7 percent, respectively, during 1980, 1981, and 1982.

Rice producers who are unaffected by cancellation of 2,4,5-T would receive net benefits from cancellation of 2,4,5-T since their production and costs would be unaffected while prices received and acres planted, responding to lower U.S. rice production, would increase above projected 1979-1990 levels. The value of production on unaffected acreage (if 2,4,5-T were cancelled) was estimated to increase 1.4, 3.4, and 5.5 percent respectively, during 1980, 1981, and 1982. Thus, much of the negative impact of the cancellation of 2,4,5-T would be offset. At both the consumer and market level, the economic impact of the cancellation would not be significant.

F. 2,4,5-T Use on Non-crop Areas*/

(1) Current Use

2,4,5-T is registered for control of many broadleaved and herbaceous weeds[*/] in a variety of urban and rural non-crop areas such as hedgerows, storage areas, and vacant lots. 2,4,5-T is used because of its relatively low cost, the broad spectrum of weeds it controls and its selectivity for control of undesirable plant species.

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*/ "Non-crop areas" includes: airports; fences, hedgerows (not otherwise included among previously suspended uses, e.g., rights-of-way, pasture); lumber yards; refineries; non-food crop areas; storage areas; wastelands (not otherwise included among previously suspended uses, e.g., forestry); vacant lots; tank farms; industrial sites and areas (not otherwise included among previously suspended uses, e.g., rights-of-way).

Recent data on the usage of 2,4,5-T for non-crop areas is not available. However, a 1974 publication reported that 200,000 pounds a.e. of 2,4,5-T were used annually for general maintenance on 100,000 acres of grounds at industrial, commercial, and institutional sites. An additional 180,000 pounds a.e. of 2,4-D and 2,4,5-T combination products were also used annually on 90,000 acres on these sites. Even combined, this area (190,000 acres) is only 11% of the total 1.8 million acres treated with one or more of 15 chemicals for grounds maintenance on these sites.

(2) Evaluation of 2,4,5-T and Alternatives

Both chemical and non-chemical controls are available as alternatives to 2,4,5-T. Chemical alternatives include herbicides, such as 2,4-D, picloram, dicamba, AMS, and amitrole. The most comparable chemical alternatives are

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[*/] The weeds are numerous and include the following broadleaf and woody plants: pigweed, ragweed, lambsquarters, horsenettle, cocklebur, and morning glory; oaks, poplar, cottonwood, wild cherry, maple, blackberry, honeysuckle, poison ivy, and wild grape.

combination products, such as 2,4-D + picloram, or 2,4-D + dicamba. Soil sterilants, such as sodium borate or sodium chlorate, could serve as alternatives to 2,4,5-T, although their use would involve a different weed control strategy. Rather than treating the foliage or stems of weeds after they emerge, soil sterilants are applied to the soil prior to weed emergence in anticipation of a weed problem.

Mechanical methods of control, such as mowing or shearing, or manual methods could also serve as alternatives to 2,4,5-T.

The comparative efficacy of the alternatives to 2,4,5-T is not known. The spectrum of weeds controlled by any one of the alternatives is thought to be smaller than 2,4,5-T. However, 2,4,5-T's weed spectrum may be approximated fairly closely by using a combination product or by using multiple applications of different active ingredients.

Generally, no more than one treatment with 2,4,5-T is needed annually to achieve control of the problem weeds. In some circumstances, one treatment will give control for up to four years. Combination products with 2,4-D and picloram will give comparable length of control to

2,4,5-T, but other herbicides, such as 2,4-D alone or amitrole, may require more than one treatment annually. The length of control with mechanical or manual means is unknown.

To compare the cost of using 2,4,5-T with the cost of using the alternatives, several of the most likely substitutes were identified. For ground broadcast and selective foliar sprays, 2,4,5-T is commonly used alone or in various combinations with other chemicals such as 2,4-D, picloram, or dicamba. Herbicide costs for 2,4,5-T, when used alone, are about $8.00 per acre and range from about $30.00 to $44.50 per acre when used in combination with other chemicals. In comparison, material costs for combinations of 2,4-D and picloram, or 2,4-D and dicamba, the most likely alternatives, range from about $24.00 to $42.50 per acre. Material costs for other chemical alternatives range from $2.45 per acre (2,4-D) to about $67.00 per acre (glyphosphate). However, use of these latter alternatives may require successive multiple applications with the same or several other herbicides in order to achieve control comparable to that provided by using 2,4,5-T.

(3) Economic Impact Analysis

In general, effective alternatives to 2,4,5-T exist for non-crop sites. For users of 2,4,5-T combination products, economic impacts will be slight. Effective alternative combination products which provide equally long-term control at a comparable price are registered and available. Impacts on users of 2,4,5-T applied as a single active ingredient will be felt in the form of increased control costs for the combination alternatives. Most of the effective combination alternatives are more expensive than 2,4,5-T alone.

Little, if any, impact is expected on the market and consumer levels because effective alternatives are available and because the economic value of weed control on non-crop sites is very small.

V. REGULATORY DETERMINATION

Section 6(b) of FIFRA provides that the Agency may move to cancel the registration of a pesticide "[i]f it appears to the Administrator that a pesticide... when used in accordance with widespread and commonly recognized practice, generally causes unreasonable adverse effects on the environment." In effect, this "unreasonable adverse effects" standard requires a finding that the risks of each use of the pesticide exceed the benefits of use, when the pesticide is used in accordance with the terms and conditions of registration or in accordance with widespread and commonly recognized practice.

Upon concluding the RPAR review of a pesticide, if the Administrator determines that the risks of use outweigh the benefits of use, he may issue a notice of intent to cancel or deny registration, pursuant to section 6(b)(1) or Section 3(c)(6). If, on the other hand, the Administrator determines that the use of the pesticide appears to cause unreasonable adverse effects on the environment, that there are uncertainties in the data relating to the risks and benefits of this use, and that additional data on the risks and benefits will assist the Agency in determining whether or not to cancel the pesticide, he may issue a notice of intent to hold a hearing pursuant to section 6(b)(2) of FIFRA to determine whether the registration should be cancelled or applications for registration denied. In the present instance a determination to issue a notice of intent to hold a hearing on the non-suspended uses of 2,4,5-T pursuant to section 6(b)(2) is the prudent course of action.

The foregoing review indicates that exposure to 2,4,5-T and/or TCDD may result in significant adverse effects in exposed populations. Agency analysis shows that the rice, rangeland, and non-crop uses of 2,4,5-T create opportunities for direct and indirect exposure to humans through aerial drift and/or related contamination of water, food, and environmental media. Even without quantitative*/ data on levels and routes of exposure, it is clear that any exposure, particularly in the case of TCDD, whether from a single source or cumulative sources, appears to pose risks of oncogenic, fetotoxic and/or teratogenic effects in the exposed populations. Additional data on routes of exposure, relative contribution from the several uses of the pesticide in areas of multiple use, and mechanisms for reducing exposure would assist the Agency in assessing with greater precision the degree of hazard associated with the non-suspended uses of 2,4,5-T.

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*/ Because of the many varied and widespread uses of silvex and 2,4,5-T, it is difficult to ascribe residue to any one particular use.

The estimated impact on farm income and beef prices of cancelling 2,4,5-T on range would be slight. When compared with the U.S. total farm value of beef production (about $15 billion annually), these impacts are relatively small (0.1 percent), averaging less than $16.5 million annually. In those localized areas where target weed species are a problem, local farm income may be affected significantly. Adequate information to evaluate such local impacts is not available. At the retail level the consumer price index for food and beverages could increase by a maximum of 0.05 percent, an insignificant increment.

If 2,4,5-T is cancelled for use on rice, annual producer weed control cost increases and production losses without 2,4,5-T are estimated at about $6 million per year. Prices received by farmers, and ultimately paid by consumers, could increase by about five percent within three years.

Since rice comprises only a small portion of the U.S. consumers' diet (consumption of milled rice is less than eight pound per capita annually), price increases of this magnitude will have only minor impacts on consumers.

Both chemical and non-chemical controls are available as alternatives to 2,4,5-T for weed control in non-crop areas. The chemical alternatives include 2,4-D, picloram, dicamba, AMS, and amitrole. Non-chemical controls include mechanical methods, such as mowing or shearing, and manual methods. The relative efficacy of the alternatives in comparison to 2,4,5-T is unknown. However, it is believed that chemical alternatives, either in multiple applications or in combination, will be widely substituted for 2,4,5-T and will provide equivalent control. Potential risks associated with the increased usage of these alternative chemicals, singly or in combination, has not been addressed by the Agency.

While the benefits of 2,4,5-T use on rangeland, rice, and non-crop areas are in some respects not insubstantial, these benefits do not, in the Agency's judgment, appear to offset the risks which these uses pose to humans and the environment. Accordingly, the rangeland, rice, and non-crop uses of 2,4,5-T appear generally to cause unreasonable adverse effects on the environment.

Because of uncertainties and incomplete data relating to some of the factors which enter into the risk-benefit analysis, the Agency is seeking additional data on these 2,4,5-T uses before making a final regulatory determination.

FIFRA provides for the resolution of such questions through public hearings held pursuant to section 6(b)(2). Through the hearing process, the uncertain areas become subject to public debate, new information is collected, and the Agency is able to arrive at an informed decision.

Moreover, in this case, a section 6(b)(2) hearing is particularly appropriate because section 6(b)(1) hearings on the suspended uses of 2,4,5-T are currently in progress. Because many of the issues to be reviewed and resolved are generic to both the suspended and the non-suspended 2,4,5-T uses, information and approaches developed for one category may shed additional light on the other category. Thus, a section 6(b)(2) hearing merged with the ongoing 6(b)(1) hearing would allow consolidated debate and disposition regarding all 2,4,5-T uses.

2,4,5-T: Position Document 2/3

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